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(74) Agents: GREENMAN, Jeffrey, M. et al.; Bayer Pharma-
ceuticals Corporation, 400 Morgan Lane, West Haven, CT
06516 (US).

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(71) Applicant (for all designated States except US): BAYER
PHARMACEUTICALS CORPORATION [US/US];
400 Morgan Lane, West Haven, CT 06516 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): CHEN, Yuanwei
[US/US]; 15 Blue Ridge Lane, North Haven, CT 06473
(US). O'CONNOR, Stephen, James [US/US]; 977 Little
Meadow Road, Guilford, CT 06437 (US). GUNN, David
[US/US]; 40 Wood Street, Hamden, CT 06517 (US).
NEWCOM, Jason [US/US]; 408 Fountain Street, Unit A,
New Haven, CT 06515 (US). CHEN, Jianqing [CA/US];
117 Frederick Street, Apt. #2-L, New Haven, CT 06515
(US). YI, Lin [CN/US]; 58 Magnolia Road, Milford, CT
06460 (US). ZHANG, Hai-Jun [CN/US]; 260 Pine Street,
Middletown, CT 06457 (US). HUNYADI, Laszlo, Matyas
[US/US]; 153 Willow Street, Apt. 1R, New Haven, CT
06511 (US). NATERO, Reina [US/US]; 416 Waverley
Street, Apt. 1, Menlo Park, CA 94025 (US).

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(54) Title: SUBSTITUTED 3,5-DIHYDRO-4H-IMIDAZOL-4-ONES FOR THE TREATMENT OF OBESITY

(57) Abstract: This invention relates to substituted 3,5-dihydro-4H-imidazol-4-ones compounds which are useful in the treatment of obesity and obesity-related disorders, and as weight-loss and weight-control agents. The invention also provides methods for synthesis of the compounds, pharmaceutical compositions comprising the compounds, and methods of using such compositions for inducing weight loss and treating obesity and obesity-related disorders.

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**SUBSTITUTED 3,5-DIHYDRO-4H-IMIDAZOL-4-ONES
FOR THE TREATMENT OF OBESITY**

[001] This application claims benefit of U.S. Provisional Application Serial No. 60/435,429, filed December 20, 2002, the contents of which are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

[002] This invention relates to substituted 3,5-dihydro-4H-imidazol-4-ones compounds which are useful in the treatment of obesity and obesity-related disorders, and as weight-loss and weight-control agents.

BACKGROUND OF THE INVENTION

[003] Obesity, which is defined as an excess of body fat relative to lean body mass, is a well-established risk factor for a number of potentially life-threatening diseases such as atherosclerosis, hypertension, diabetes, stroke, pulmonary embolism, sleep apnea, and cancer. Furthermore, it complicates numerous chronic conditions such as respiratory diseases, osteoarthritis, osteoporosis, gall bladder disease, and dyslipidemias. The enormity of this problem is best reflected in the fact that death rates escalate with increasing body weight. More than 50% of all-cause mortality is attributable to obesity-related conditions once the body mass index (BMI) exceeds 30 kg/m², as seen in 35 million Americans (Lee, JAMA 268:2045-2049, 1992). By contributing to greater than 300,000 deaths per year, obesity ranks second only to tobacco smoking as the most common cause of potentially preventable death (McGinnis, JAMA 270:2207-2212, 1993). Accompanying the devastating medical consequences of this problem is the severe financial burden placed on the health care system in the United States. It is estimated that 30-50% of the middle-age population may be considered as obese (Kuczmarski et al., JAMA 272:205-211, 1994). The economic impact of obesity and its associated illnesses from medical expenses and loss of income are reported to be in excess of \$68 billion/a year (Colditz, Am. J. Clin. Nutr. 55:503S-507S, 1992). This figure does not include the greater than \$30 billion per year spent on weight loss foods, products, and programs (Wolf, Pharmacoeconomics. 5:34-37, 1994).

[004] The accumulation or maintenance of body fat bears a direct relationship to caloric intake. Comprehensive treatment programs, therefore, focused on behavior modifications to reduce caloric intake and increase physical activity using a myriad of systems. These methods have limited efficacy and are associated with recidivism rates exceeding 95% (NIH Technology Assessment Conference Panel, Ann. Intern. Med. 119:764-770, 1993).

[005] Obesity has also been treated by administering specific agents, for example, anorectic agents, to obese subjects. However, anorectic agents such as dextroamphetamine, the combination of the non-amphetamine drugs phentermine and fenfluramine (Phen-Fen), and dexfenfluramine

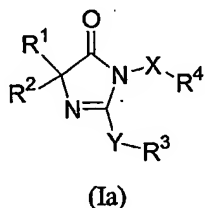
(Redux) alone, are associated with serious side effects. Indigestible materials such as olestra (OLEAN[®], mineral oil or neopentyl esters, U.S. Patent No. 2,962,419) have been proposed as substitutes for dietary fat. Garcinia acid and derivatives thereof have been described as treating obesity by interfering with fatty acid synthesis. Swellable crosslinked vinyl pyridine resins have been described as appetite suppressants via the mechanism of providing non-nutritive bulk (*see, e.g.*, U.S. Patent No. 2,923,662).

[006] Surgical interventions, such as gastric partitioning procedures, jejunoileal bypass, and vagotomy, have also been developed to treat severe obesity (Greenway, *Endo. Metab. Clin. N. Amer.* 25:1005-1027, 1996). Although these surgical procedures are somewhat more effective in the long run, the acute risk benefit ratio has reserved these invasive procedures for morbidly obese patients according to the National Health Institutes (NIH) consensus conference on obesity surgery (BMI > 40 kg/m²) (NIH Conference, *Ann. Intern. Med.* 115:956-961, 1991). Therefore, this approach is not an alternative for the majority of overweight patients unless and until they become profoundly obese and are suffering the attendant complications.

[007] Thus, new methods and compositions that promote weight-loss are urgently needed.

DESCRIPTION OF THE INVENTION

[008] The invention pertains to substituted 3,5-dihydro-4*H*-imidaz-5-one compounds of Formula (Ia) and pharmaceutical salts and esters thereof. In particular, the invention pertains to a compound of Formula (Ia)



wherein

R¹ and R² are independently selected from

(C₁-C₆)alkyl,

thienyl,

pyridyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)alkoxy,

(C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy, and

phenyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)alkoxy,

(C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy,

and

when R^1 and R^2 are each (C_1-C_6) alkyl, they can be taken together with the carbon atom to which they are attached to form a saturated 5- or 6-membered carbocyclic ring;

Y is $(CH_2)_n$;

n is 0 or 1;

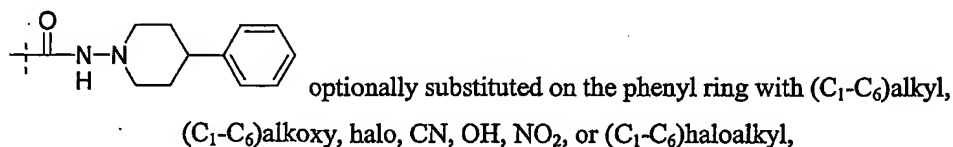
R^3 is independently selected from

H,
 (C_1-C_6) alkyl,
 NR^8R^9 ,
 (C_1-C_6) alkoxy,
 (C_3-C_8) cycloalkyl,
pyridyl optionally substituted up to 3 times with (C_1-C_6) alkyl, (C_1-C_6) alkoxy, CN, halo, (C_1-C_6) haloalkyl, or (C_1-C_6) haloalkoxy,
phenyl optionally substituted up to 3 times with (C_1-C_6) alkyl, (C_1-C_6) alkoxy, CN, halo, (C_1-C_6) haloalkyl, or (C_1-C_6) haloalkoxy,
thienyl optionally substituted up to 3 times with (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halo, or (C_1-C_6) haloalkyl,
morpholinyl,
piperidyl, and
pyrolidinyl;

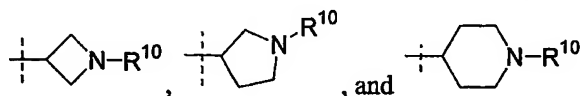
X is represents a linker selected from

a bond,
and
a (C_1-C_5) alkyl chain optionally substituted with F, OH, alkoxy, CO_2R^5 , $C(O)R^6$, oxo, or $C(O)NHR^7$;

R^4 is selected from

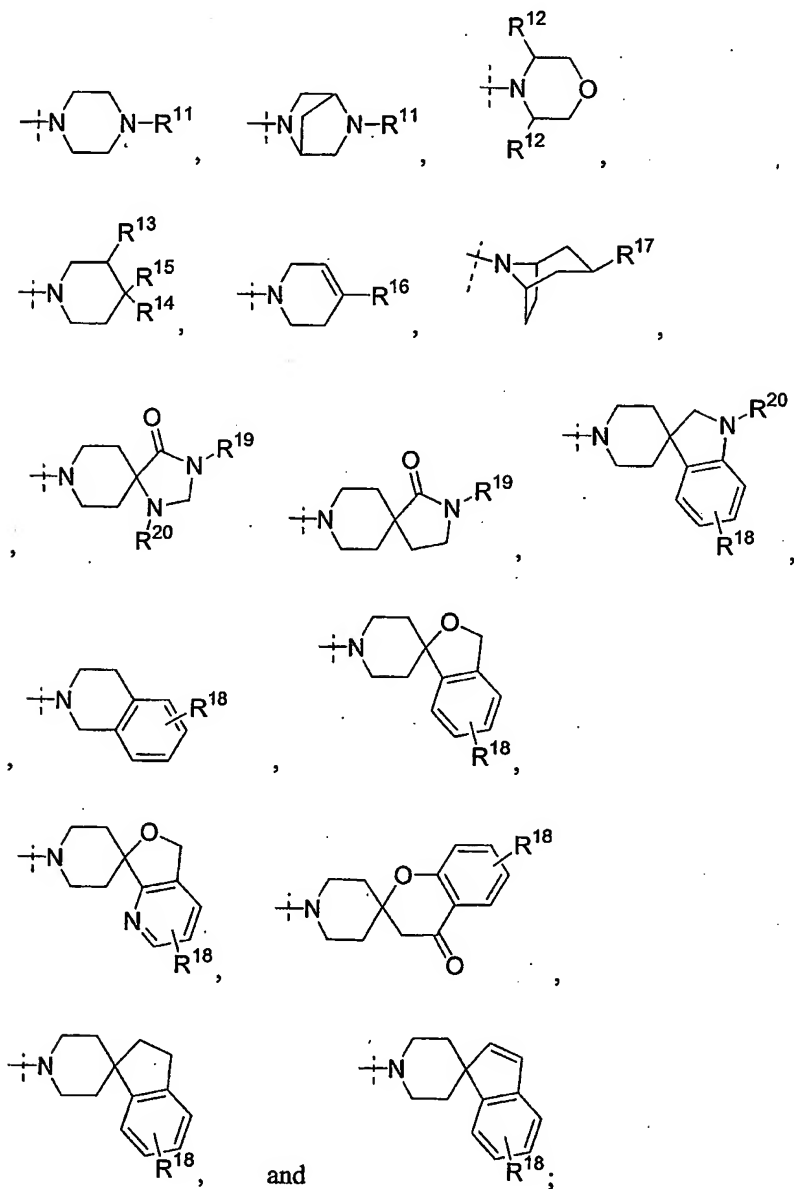


a 4-6-membered saturated heterocyclic ring selected from



and

a saturated or partially unsaturated, monocyclic, bicyclic, or spiroannulated heterocyclic ring radical selected from



R^5 is H or (C_1-C_6) alkyl;

R^6 is (C_3-C_8) cycloalkyl or (C_1-C_6) alkyl optionally substituted by phenyl;

R^7 is H or (C_1-C_6) alkyl;

R⁸ and R⁹ are independently selected from

H,
phenyl optionally substituted with CN, (C₁-C₆)alkyl, halo, (C₁-C₆)alkoxy, COR⁶,
(C₁-C₆)haloalkyl, or NR⁵R⁷,
(C₃-C₈)cycloalkyl, and
(C₁-C₆)alkyl optionally substituted with halo, phenyl, (C₁-C₆)alkoxy, or OH;

R¹⁰ is selected from

H,
CO₂R⁶,
(C₁-C₆)alkyl optionally substituted by
phenyl optionally substituted with (C₁-C₆)alkyl,
indolyl,
dihydrobenzofuryl or benzofuryl optionally substituted with halo,
benzothienyl optionally substituted with halo,
benzimidazolyl,
chromenyl optionally substituted with methoxy, nitro, oxo, hydroxy, halo, or
(C₁-C₆)alkyl,
methylenedioxyphenyl,
pyridyl, and
isoxazolyl optionally substituted with phenyl or (C₁-C₆)alkyl);

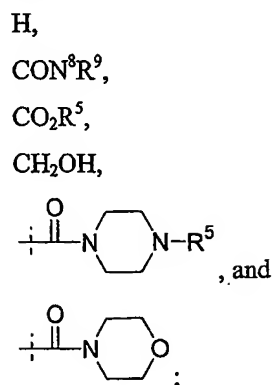
R¹¹ is selected from

H,
pyrimidyl,
(C₁-C₆)alkyl, and
pyridyl optionally substituted with CN, (C₁-C₆)alkyl, halo, (C₁-C₆)alkoxy, COR⁶,
(C₁-C₆)haloalkyl, or NR⁸R⁹, and
phenyl optionally substituted with CN, (C₁-C₆)alkyl, halo, (C₁-C₆)alkoxy, COR⁶,
(C₁-C₆)haloalkyl, or NR⁸R⁹;

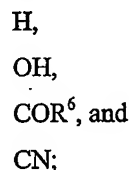
R¹² is independently selected from

H, and
(C₁-C₆)alkyl;

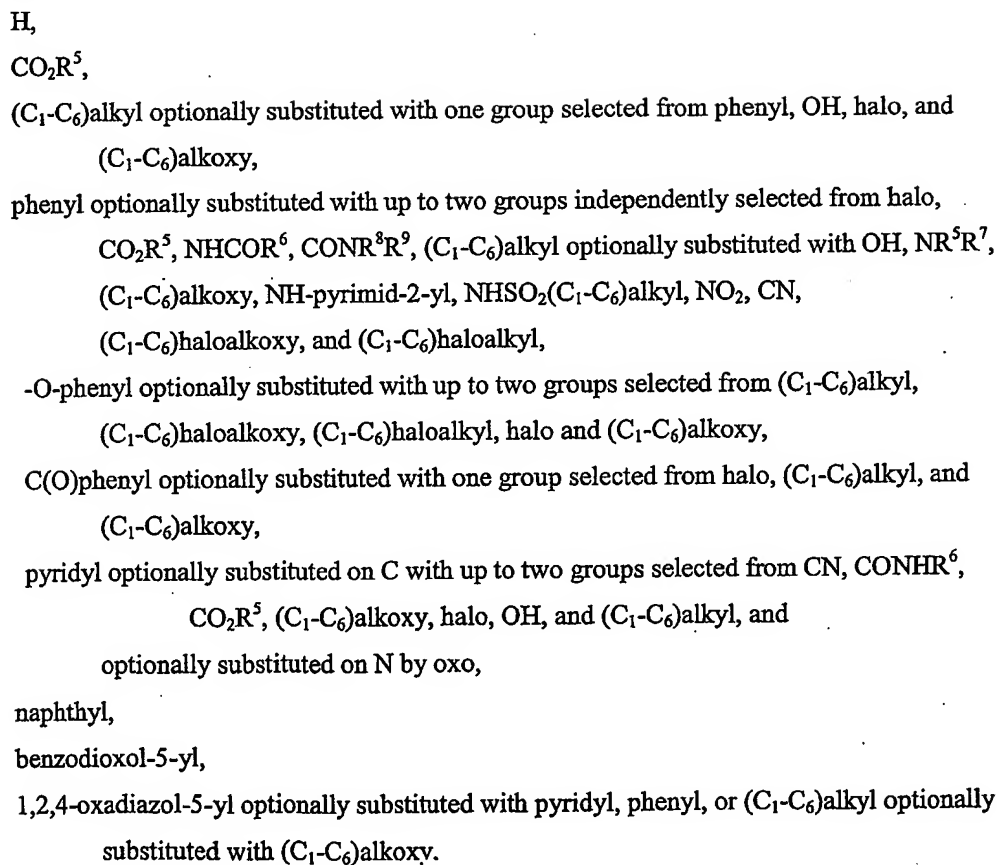
R¹³ is selected from



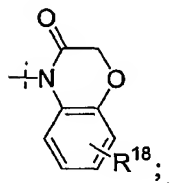
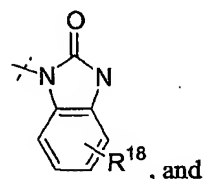
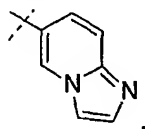
R¹⁴ is selected from



R¹⁵ is selected from



1,2,4-oxadiazol-3-yl optionally substituted with (C₁-C₆)alkyl, pyridyl, or phenyl,
 benzotriazolyl,
 pyrimidyl optionally substituted with OR⁵, (C₁-C₆)alkyl, phenyl, or pyridyl,
 indolyl,
 benzimidazolyl,
 quinolinyl optionally substituted with halo or CF₃,
 benzodioxanyl,



R¹⁶ is selected from

H,

(C₁-C₆)alkyl,

phenyl optionally substituted with up to two groups independently selected from halo,
 CO₂R⁵, NHCOR⁶, CONR⁸R⁹, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, NH₂, NO₂, CN, and
 CF₃, and

pyridyl optionally substituted with up to two groups independently selected from halo,
 CO₂R⁵, NHCOR⁶, CONR⁸R⁹, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, NH₂, NO₂, CN, and
 CF₃;

R¹⁷ is selected from

H,

(C₁-C₆)alkyl, and

phenyl optionally substituted with up to two groups independently selected from halo,
 CO₂R⁵, NHCOR⁶, CONR⁸R⁹, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, NH₂, NO₂, CN, and
 CF₃;

R¹⁸ is selected from H, halo, CN, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkyl;

R¹⁹ is H, (C₁-C₆)alkyl, or phenyl;

R²⁰ is selected from

H,

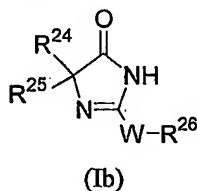
CO₂(C₁-C₆)alkyl optionally substituted with phenyl(CO₂-benzyl),

SO₂CH₃, and

phenyl;

and pharmaceutically salts thereof.

[009] The invention also pertains to a compound of Formula (Ib)



wherein

R²⁴ and R²⁵ are independently selected from

(C₁-C₆)alkyl,

thienyl,

pyridyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl,

(C₁-C₆)haloalkoxy, (C₁-C₆)alkoxy, and

phenyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl,

(C₁-C₆)haloalkoxy, (C₁-C₆)alkoxy,

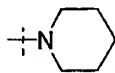
and

when R²⁴ and R²⁵ are each (C₁-C₆)alkyl, they can be taken together with the carbon atom to which they are attached to form a saturated 5- or 6-membered carbocyclic ring;

W is (CH₂)_p;

p is 3, 4, or 5;

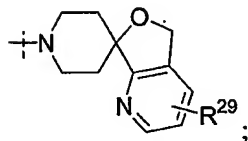
R²⁶ is selected from



optionally substituted with

phenyl optionally substituted with halo, CN, (C₁-C₆)haloalkoxy,
 (C₁-C₆)haloalkyl, (C₁-C₆)alkyl, CH, (C₁-C₆)alkoxy, or NR²⁷R²⁸,
 pyridyl optionally substituted with halo, (C₁-C₆)haloalkyl, (C₁-C₆)alkyl,
 CH, (C₁-C₆)alkoxy, NR²⁷R²⁸, or
 up to three (C₁-C₆)alkyl groups,

and



R²⁷ and R²⁸ are independently selected from

H,
 phenyl optionally substituted with CN, (C₁-C₆)alkyl, halo, (C₁-C₆)alkoxy, CO(C₁-C₆)alkyl,
 (C₁-C₆)haloalkyl, NH₂, N[(C₁-C₆)alkyl]₂, or NH(C₁-C₆)alkyl,
 (C₃-C₈)cycloalkyl, and
 (C₁-C₆)alkyl optionally substituted with halo, phenyl, (C₁-C₆)alkoxy or OH;

and

R²⁹ is H, halo, CN, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, or (C₁-C₆)haloalkyl;

and pharmaceutically salts thereof.

DEFINITIONS

[010] The terms identified above have the following meaning throughout:

The term "halo" means F, Cl, Br, or I.

[011] The term "(C₁-C₆) alkyl" means a straight or branched saturated hydrocarbon carbon chain of from 1 to about 6 carbon atoms, respectively. Examples of such groups include methyl, ethyl, isopropyl, sec-butyl, 2-methylpentyl, n-hexyl, and the like.

[012] The term “(C₁-C₆)haloalkyl” means a C₁-C₆ alkyl group substituted by 1 to 3 halogen atoms or fluorine up to the perfluoro level. Examples of such groups include trifluoromethyl, tetrafluoroethyl, 1,2-dichloropropyl, 5-bromopentyl, 6-iodohexyl, and the like.

[013] The term “(C₃-C₈)cycloalkyl” means a saturated carbocyclic ring system of from 3 to about 8 carbon atoms. Examples of such groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like.

[014] The term “(C₁-C₆)acyl” means a C₁-C₆ alkyl group attached at the carbonyl carbon atom. The radical is attached to the rest of the molecule at the carbonyl bearing carbon atom. Examples of such groups include acetyl, propionyl, n-butanoyl, 2-methylpentantoyl, and the like.

[015] The term “(C₁-C₆)alkoxy” mean a linear or branched saturated carbon group having from 1 to about 6 C atoms, respectively, and said carbon group being attached to an O atom. The O atom is the point of attachment of the alkoxy substituent to the rest of the molecule. Such groups include, but are not limited to, methoxy, ethoxy, *n*-propoxy, isopropoxy, and the like.

[016] The term “(C₁-C₆)haloalkoxy” means a C₁-C₆ alkoxy group further substituted on C with 1 to 3 halogen atoms or fluorine up to the perfluoro level.

[017] The term “optionally substituted” means that, unless indicated otherwise, the moiety so modified may have from one to up to the number of substituents indicated, provided the resulting substitution is chemically feasible as recognized in the art. Each substituent may replace any H atom on the moiety so modified as long as the replacement is chemically possible and chemically stable. For example, a chemically unstable compound would be one where each of two substituents is bonded to a single C atom through each substituents heteroatom. Another example of a chemically unstable compound would be one where an alkoxy group is bonded to the unsaturated carbon of an alkene to form an enol ether. When any moiety is described as being substituted, it can have one or more of the indicated substituents that can be located at any available position on the moiety. When there are two or more substituents on any moiety, each term shall be defined independently of any other substituent so that, accordingly, the substituents can be the same or different.

[018] As used herein, the term “substituted” is contemplated to include all permissible substituents of organic compounds. In a broad aspect, the permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described herein above. The permissible substituents can be one or more and the same or different for appropriate organic compounds. For purposes of this invention, the heteroatoms such as nitrogen may have hydrogen substituents and/or any permissible substituents of organic compounds

described herein which satisfy the valences of the heteroatoms. This invention is not intended to be limited in any manner by the permissible substituents of organic compounds.

[019] The term "analog" of a compound refers to a compound having a substantial structural similarity to a particular compound and having essentially the same biological activity as the compound.

[020] The term "derivative" of a compound or of a small molecule refers to a compound which can be derived, for example, by chemical synthesis, from the original compound. Thus a derivative of a compound has certain structural similarities with the compound.

[021] The phrase "protecting group" as used herein means temporary substituents which protect a potentially reactive functional group from undesired chemical transformations. Examples of such protecting groups include esters of carboxylic acids, silyl ethers of alcohols, and acetals and ketals of aldehydes and ketones, respectively. The field of protecting group chemistry has been reviewed (Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, 2nd ed.; Wiley: New York, 1991).

[022] For purposes of this invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 67th Ed., 1986-87. Also for purposes of this invention, the term "hydrocarbon" is contemplated to include all permissible compounds having at least one hydrogen and one carbon atom. In a broad aspect, the permissible hydrocarbons include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and nonaromatic organic compounds which can be substituted or unsubstituted.

[023] Representative salts of the compounds of Formulae (Ia) and (Ib) include the conventional non-toxic salts and the quaternary ammonium salts which are formed, for example, from inorganic or organic acids or bases by means well known in the art. For example, such acid addition salts include acetate, adipate, alginate, ascorbate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, citrate, camphorate, camphorsulfonate, cinnamate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, itaconate, lactate, maleate, mandelate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, nitrate, oxalate, pamoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, sulfonate, tartrate, thiocyanate, tosylate, and undecanoate.

[024] Base salts include alkali metal salts such as potassium and sodium salts, alkaline earth metal salts such as calcium and magnesium salts, and ammonium salts with organic bases such as dicyclohexylamine salts and *N*-methyl-D-glucamine. Additionally, basic nitrogen containing

groups may be quaternized with such agents as lower alkyl halides such as methyl, ethyl, propyl, and butyl chlorides, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, and dibutyl sulfate; and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl, and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides and others.

[025] The esters in the present invention are non-toxic, pharmaceutically acceptable ester derivatives of the alcohols of Formulae (Ia) and (Ib). This includes ester derivatives prepared from acetic, benzoic, mandelic, stearic, lactic, salicylic, hydroxynaphthoic, glucoheptonic, and gluconic acid. The alcohol compounds of Formulae (Ia) and (Ib) may be esterified by a variety of conventional procedures including reacting the appropriate anhydride, carboxylic acid, or acid chloride with the alcohol group of the respective Formulae (Ia) or (Ib) compound. The appropriate anhydride is reacted with the alcohol in the presence of an acylation catalyst such as 1,8-bis[dimethylamino]naphthalene or DMAP (*N,N*-dimethylaminopyridine). An appropriate carboxylic acid may be reacted with the alcohol in the presence of a dehydrating agent such as dicyclohexylcarbodiimide, 1-[3-dimethylaminopropyl]-3-ethylcarbodiimide or other water soluble dehydrating agents which are used to drive the reaction by the removal of water, and optionally, an acylation catalyst. Esterification may also be reached using the appropriate carboxylic acid in the presence of trifluoroacetic anhydride and optionally, pyridine, or in the presence of *N,N*-carbonyldiimidazole with pyridine. Reaction of an acid chloride with the alcohol may be carried out with an acylation catalyst such as DMAP or pyridine. One skilled in the art would readily know how to successfully carry out these as well as other methods of esterification of alcohols. Sensitive or reactive groups on the compound of Formulae (Ia) and (Ib) may need to be protected during any of the above methods for forming esters, and protecting groups may be added and removed by conventional methods well known in the art.

[026] It will be appreciated that diastereomers and enantiomers of the exemplified structures will often be possible, and that pure isomers represent preferred embodiments. It is intended that pure stereoisomers, and mixtures thereof, are within the scope of the invention.

[027] The compounds of this invention may, either by nature of asymmetric centers or by restricted rotation, be present in the form of isomers. Any isomer may be present in the (*R*)-, (*S*)-, or (*R,S*) configuration, preferably in the (*R*)- or (*S*)- configuration, whichever is most active.

[028] All isomers, whether separated, pure, partially pure, or in racemic mixture, of the compounds of this invention are encompassed within the scope of this invention. The purification of said isomers and the separation of said isomeric mixtures may be accomplished by standard techniques known in the art.

[029] Geometric isomers by nature of substituents about a double bond or a ring may be present in cis (= *Z*-) or trans (= *E*-) form, and both isomeric forms are encompassed within the scope of this invention.

[030] The particular process to be utilized in the preparation of the compounds of this invention depends upon the specific compound desired. Such factors as the selection of the specific moieties and the specific substituents on the various moieties, all play a role in the path to be followed in the preparation of the specific compounds of this invention. These factors are readily recognized by one of ordinary skill in the art.

[031] For synthesis of any particular compound, one skilled in the art will recognize that the use of protecting groups may be required for the synthesis of compounds containing certain substituents. A description of suitable protecting groups and appropriate methods of adding and removing such groups may be found in: *Protective Groups in Organic Synthesis*, Second Edition, T. W. Greene, John Wiley and Sons, New York, 1991.

[032] In the Reaction Schemes 1-19 described below, one skilled in the art will recognize that reagents and solvents actually used may be selected from several reagents and solvents well known in the art to be effective equivalents. When specific reagents or solvents are shown in a Reaction Scheme, therefore, they are meant to be illustrative examples of conditions desirable for the execution of that particular Reaction Scheme.

GENERAL METHODS OF PREPARATION OF FORMULAE (Ia) and (Ib) COMPOUNDS

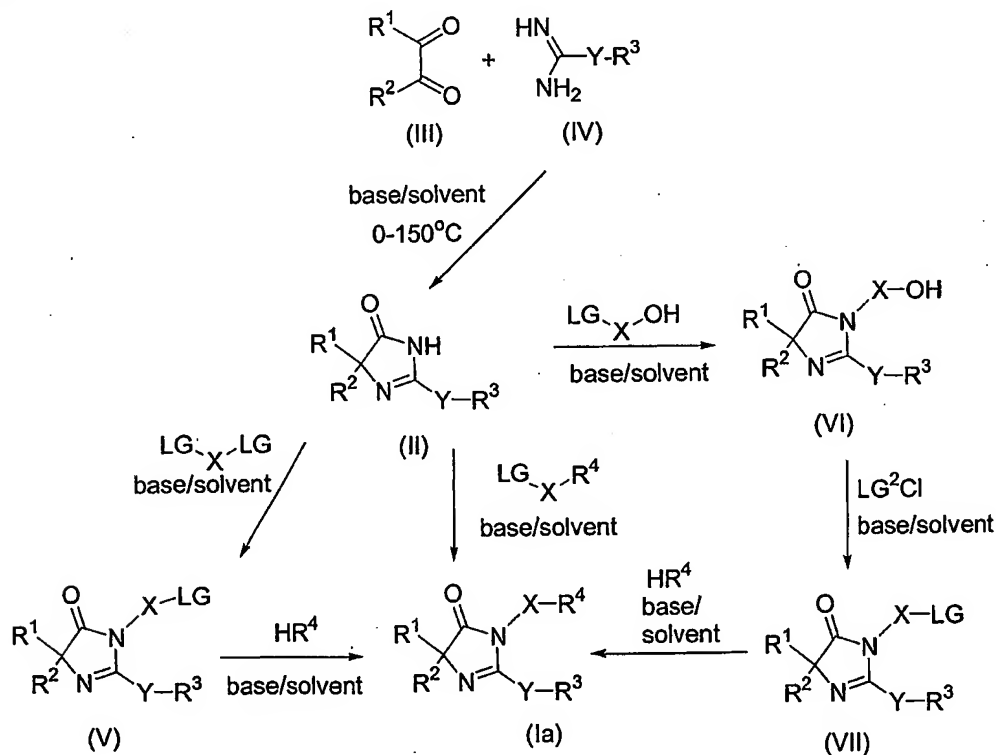
[033] In general, Formulae (Ia) and (Ib) compounds may be prepared by standard techniques known in the art and by known processes analogous thereto. In particular, seven such standard methods may be used, the selection of which may be based, among other considerations, upon the availability of the required individual starting materials. These seven methods are illustrated in Reaction Schemes 1, 2, 3, 5, 8, 9, and 10 below.

[034] Additional compounds of Formulae (Ia) and (Ib) may be prepared from other Formulae (Ia) and (Ib) compounds by elaboration of functional groups present. Such elaboration includes, but is not limited to, hydrolysis, reduction, oxidation, alkylation, acylation, esterification, amidation, and dehydration reactives. Such transformations may in some instances require the use of protecting groups by the methods disclosed in T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*; Wiley: New York, (1999), and incorporated herein by reference. Such methods would be initiated after synthesis of the desired compound or at another place in the synthetic route that would be readily apparent to one skilled in the art.

[035] The compounds of Formula (Ia) where each variable may be any moiety within that variable's definition can be synthesized according to Reaction Scheme 1, wherein an appropriate

diketone (III) is allowed to react with the appropriate amidine (IV) (commercially available or prepared by Reaction Scheme 5) to provide cyclic intermediate (II). This cyclization step is typically carried out in a base at rt to 150°C, and in an aprotic solvent such as dimethyl sulfoxide, dimethyl formamide, acetonitrile, acetone, dioxane, or an alcohol such as ethanol, isopropanol, n-propanol, n-butanol, iso-butanol, and t-butanol. The base is typically one of the following base such as Cs₂CO₃, K₂CO₃, Na₂CO₃, K₃PO₄, Na₃PO₄, NaOH, KOH, NaH, or a sodium or potassium alkoxide. The intermediate (II) may then be converted into compounds of Formula (Ia) by alternative routes. The first route is alkylation of (II) under basic conditions with an appropriate alkylation reagent and represented by the Formula LG-X-R⁴. Alternatively, (II) can be reacted with alkyl dihalide to provide intermediate (V), which is reacted with HR⁴ under basic conditions to provide (Ia). Finally, intermediate (II) is allowed to react with an alcohol containing a leaving group (i.e., LG-X-OH) to produce intermediate (VI), which is converted to a mesylate or tosylate, and allowed to further react with HR⁴ to provide compound (Ia).

[036]

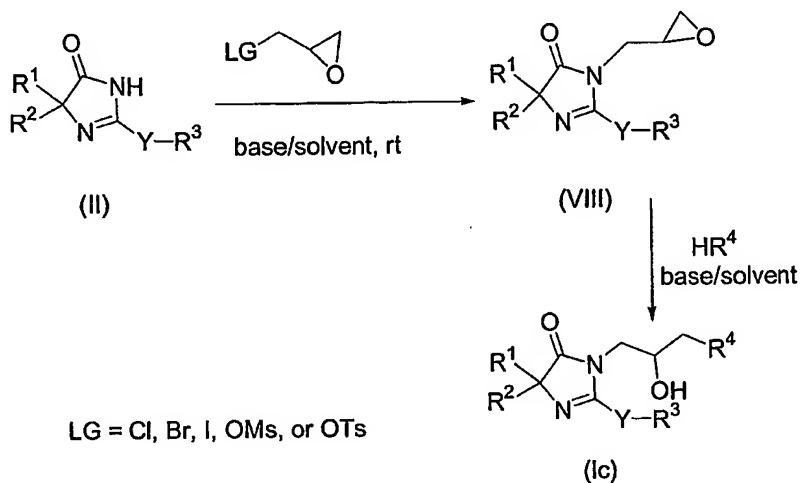
REACTION SCHEME 1

LG = Cl, Br, I, OMs, or OTs

LG² = Ms or Ts

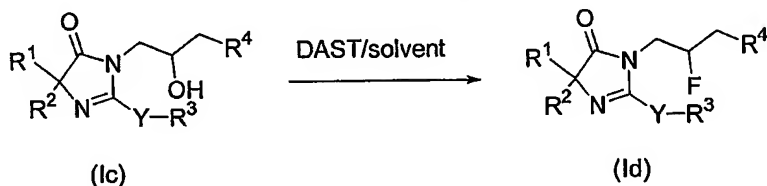
[037] Compounds of Formula (Ic) can be prepared by the reaction of (II) with an epoxide containing a leaving group (Reaction Scheme 2). The epoxide product (VIII) is then reacted with HR^4 in the basic conditions to provide (Ic).

[038]

REACTION SCHEME 2

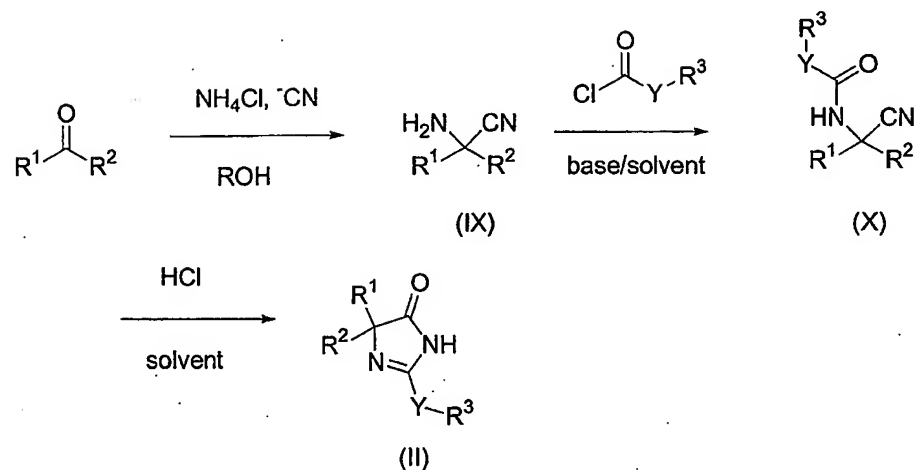
[039] A fluoro containing compound with Formula (Id) can be prepared from (Ic) by reaction of a fluorinating agent such as DAST in a solvent such as toluene or benzene (Reaction Scheme 3).

[040]

REACTION SCHEME 3

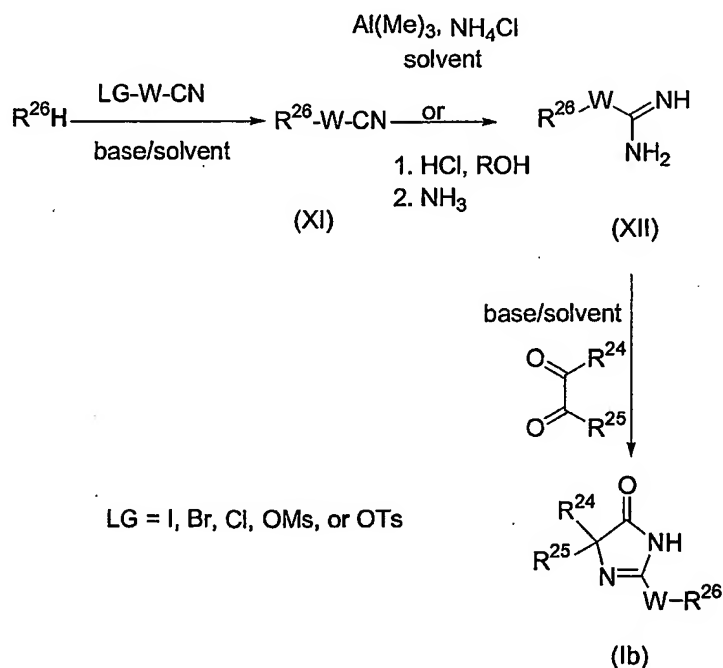
[041] The intermediate (II) may also be prepared by an alternative route as shown in Reaction Scheme 4. Typically, a ketone $\text{R}^1\text{R}^2\text{C}=\text{O}$, is subjected to the Strecker reaction conditions to provide the aminonitrile which may be acylated, and cyclized under acidic conditions to provide (II).

[042]

REACTION SCHEME 4

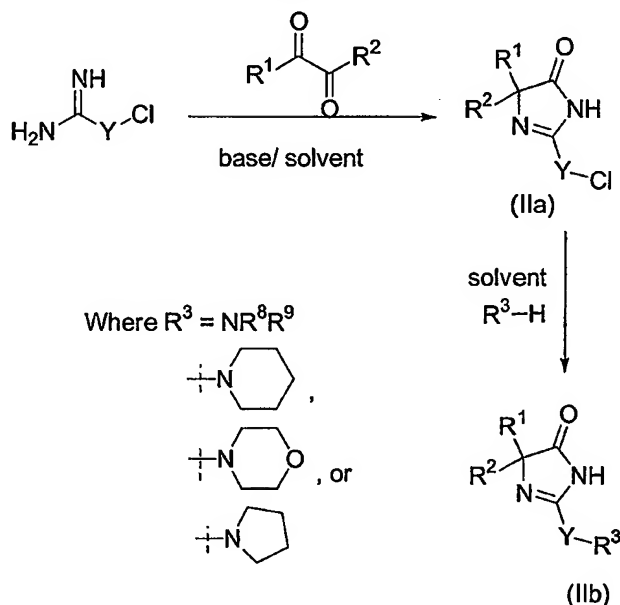
[043] The compound of Formula (Ib) where R^{24} , R^{25} , R^{26} , and W , as defined above, can be prepared by the method shown in Reaction Scheme 5. Thus, $R^{26}H$ is reacted with a nitrile containing a leaving group to provide (XI) in the standard alkylation conditions. The nitrile is then converted to an amidine (XII) under Louis acid conditions, which is further reacted with a diketone to provide (Ib).

[044]

REACTION SCHEME 5

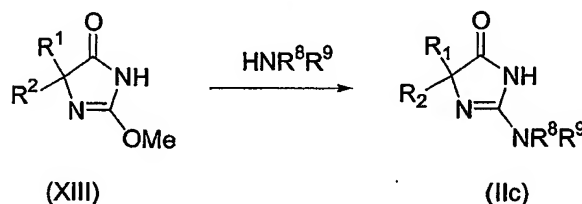
[045] The intermediate of Formula (IIb) in which Y is lower alkyl and R^3 is NR^8R^9 , morpholinyl, pyrrolidinyl, or piperidinyl, can be prepared as shown in Reaction Scheme 6. An amidine, which is either commercially available or prepared according to Reaction Scheme 5, is reacted with diketone to provide (IIa). The halide is replaced by the R^3 group (i.e., a primary or secondary amine) under standard conditions to provide (IIb).

[046]

REACTION SCHEME 6

[047] Similarly, (IIc) can be prepared from (XIII), prepared according to Reaction Scheme 1, and an amine, R^8R^9NH , as shown in Reaction Scheme 7.

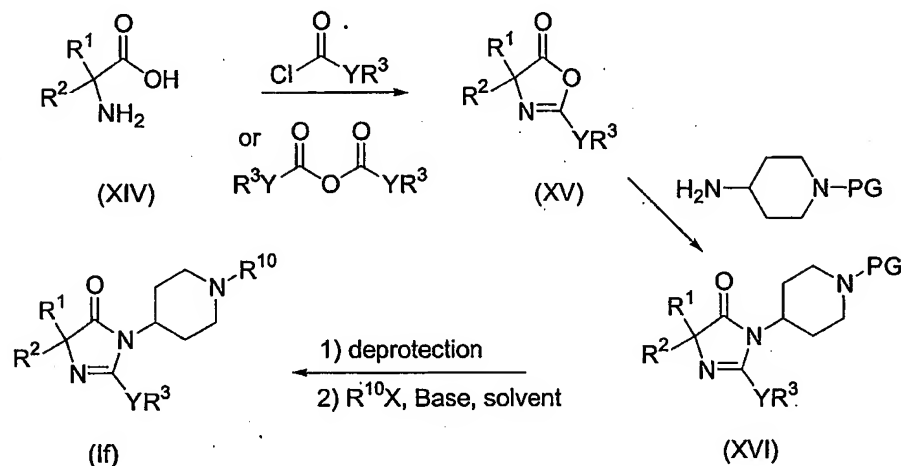
[048]

REACTION SCHEME 7

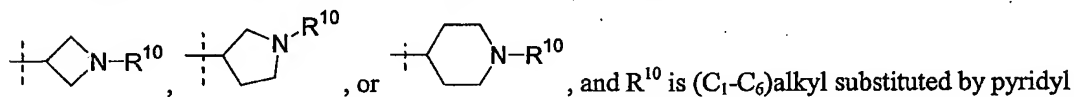
[049] The compound of Formula (If), where R^{10} is a (C_1-C_6) alkyl substituted with substituted piperidine or substituted pyrrolidine can be prepared by the route shown in Reaction Scheme 8. The amino acid (XIV), either commercially available or prepared by the standard methods, is reacted with an acyl chloride or an anhydride to provide an oxazolone (XV). Imidazolone (XVI) is

obtained by treatment of (XV) with aminopiperidine. The protecting group is removed and alkylated with an alkylation agent to provide (If).

[050]

REACTION SCHEME 8

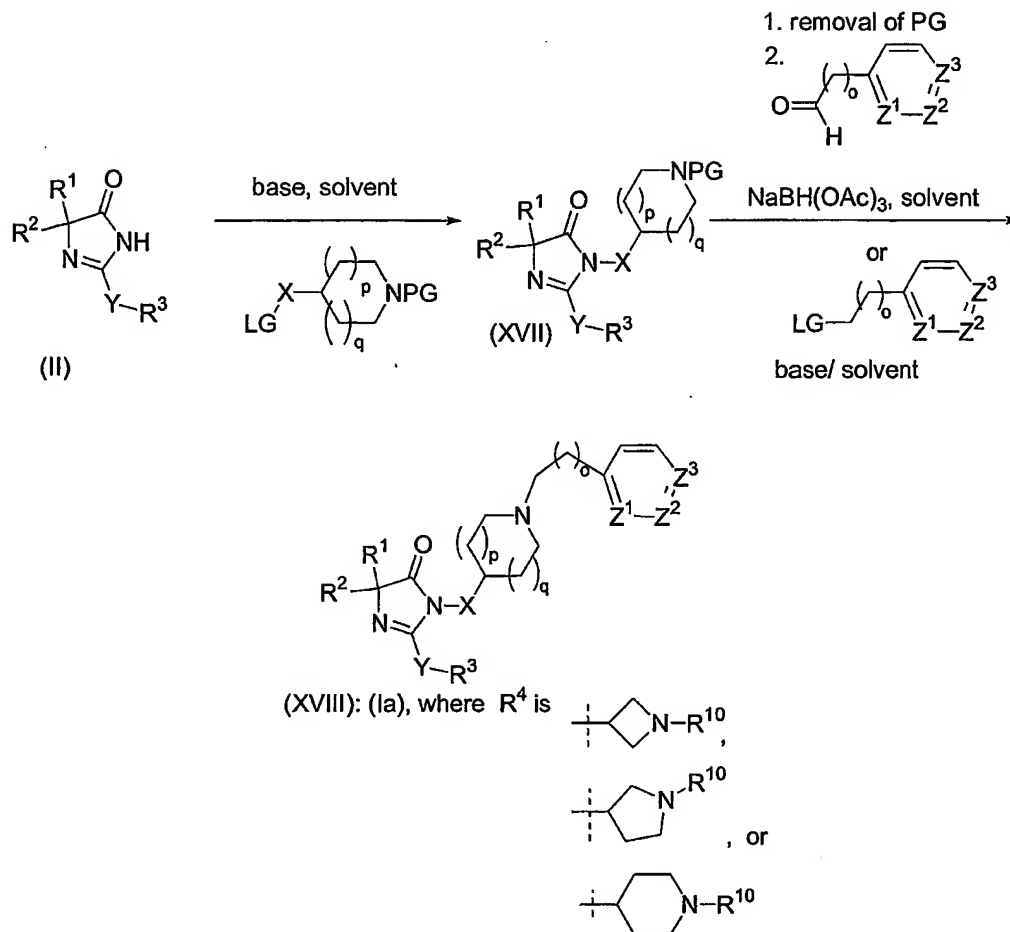
[051] Reaction Scheme 9 describes the preparation of compounds of Formula (Ia) in which R⁴ is



of phenyl, or more generally represented as Formula (XVIII) in which one of Z¹, Z², and Z³ is either a carbon or nitrogen atom; p and q are 0 or 1; and o is 0, 1, 2, 3, 4, or 5. N-alkylation of Intermediate (II) under basic conditions provides intermediate (XVII), which is converted to compound (XVIII) by reductive amination or alkylation reactions. In this scheme and in subsequent schemes, PG and PG' indicates a suitable protecting group such as BOC, added and removed as needed to facilitate the synthesis, according to standard methods known in the art.

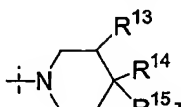
[052]

REACTION SCHEME 9

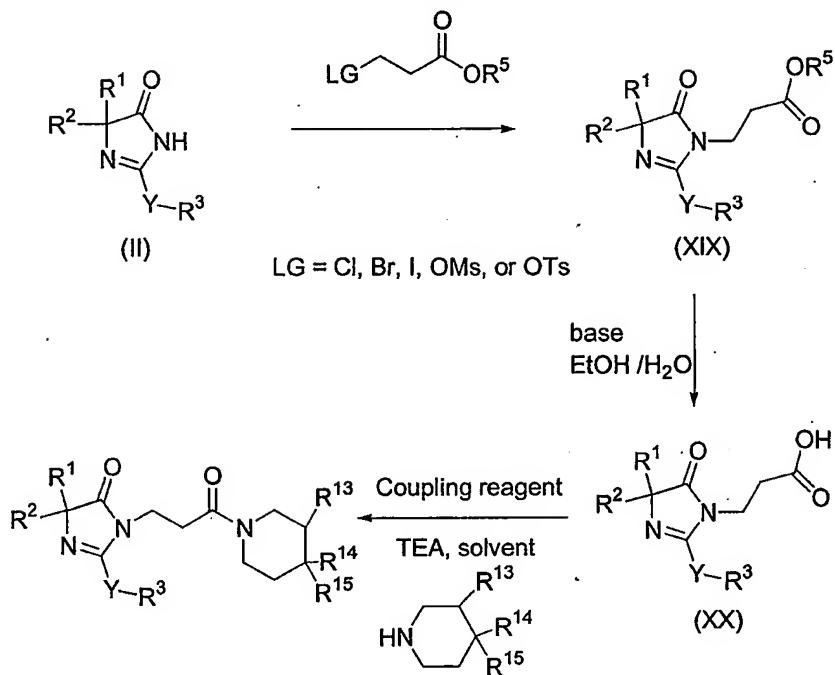


and R¹⁰ is (C₁-C₆)alkyl substituted by phenyl or pyridyl

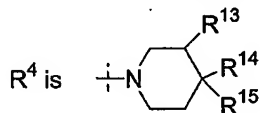
[053] The compounds of Formula (XXI) [Formula (Ia) in which X is an alkyl linker substituted by

oxo, and R⁴ is ] are prepared according to Reaction Scheme 10. Thus, (II) is alkylated with an halo-ester to provide (XIX). The ester is hydrolyzed under basic conditions to provide the free acid (XX), which is coupled with a piperidine in the presence of a coupling agent such as EDCI, to provide the amide of Formula (XXI).

[054]

REACTION SCHEME 10

(XXI): (Ia), where X is alkyl substituted by oxo,

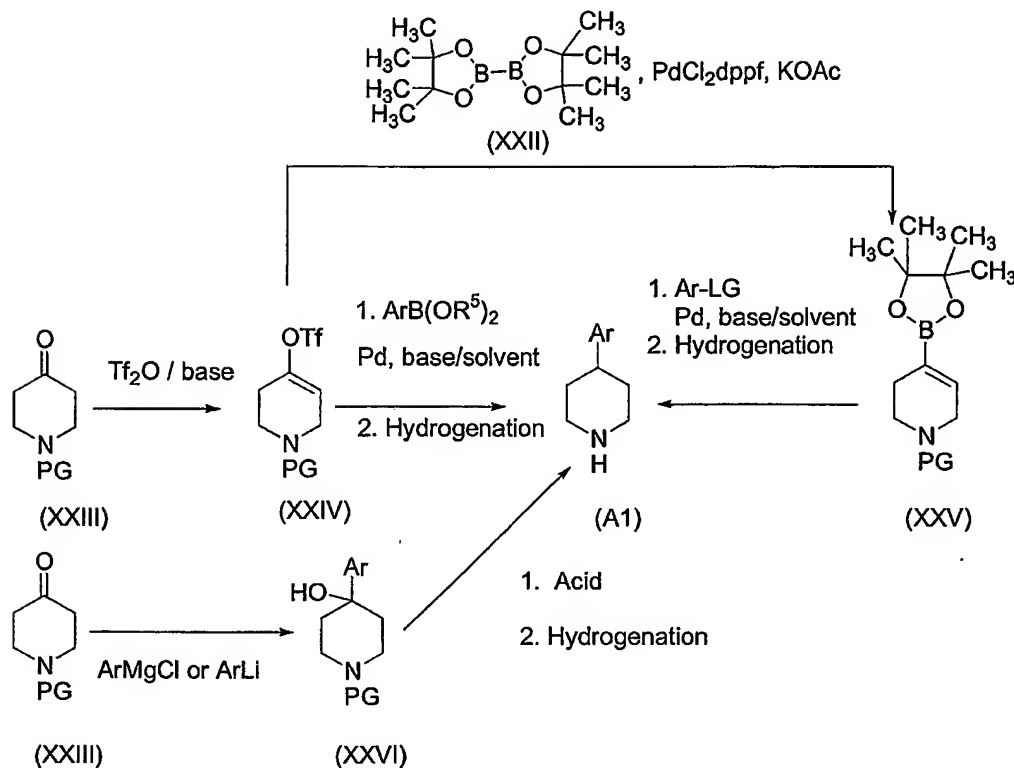
**GENERAL METHOD OF PREPARATION OF INTERMEDIATES**

[055] The starting materials required to carry out the above described reactions (piperidines, ketones, epoxides) are in many cases commercially available or can be readily prepared by methods known to those skilled in the art. The following routes are exemplary of such methods, but are not intended to be limiting in any way.

[056] The piperidines (A1) are commercially available or can be prepared according to one of the many procedures described in the literature. Some can be prepared by the reactions described below.

[057] The piperidine ketone is converted to the triflate (XXIV) under the standard conditions (Reaction Scheme 11). Piperidine substituents (e.g. R¹⁵ groups) which are aromatic such as phenyl or pyridyl, are introduced by Suzuki coupling, followed by hydrogenation and deprotection to provide (A1). Alternatively, (A1) can also be prepared by the borane (XXV), which is prepared from bis(pinacolato)diboron (XXII), under standard Suzuki coupling conditions followed by hydrogenation. Alternatively, (A1) can also be prepared by the reaction of Grignard reagent or Lithium reagent with ketone (XXIII), followed by dehydration, catalytic hydrogenation.

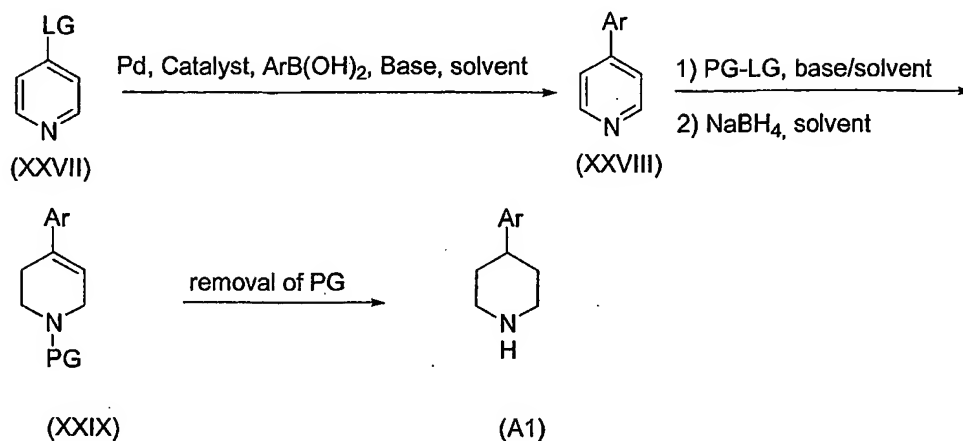
[058]

REACTION SCHEME 11

LG = Cl, Br, I, OMs, or OTs

[059] Alternatively, (A1) can be prepared according to Reaction Scheme 12. Pyridine (XXVII) can be coupled with boronic acid under Suzuki coupling conditions to provide an aryl pyridine (XXVIII), which can be reduced by a reducing agent such as NaBH_4 and the protecting group can be removed to provide the piperidine (A1).

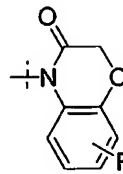
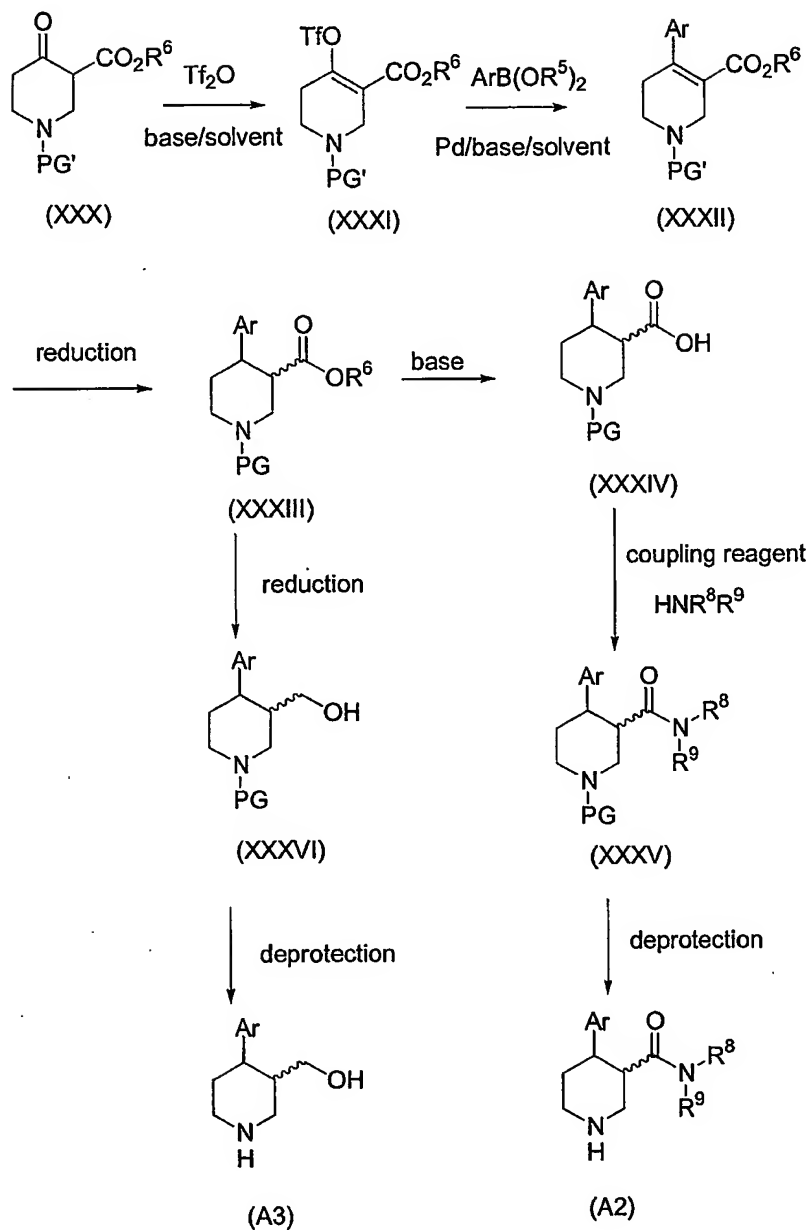
[060]

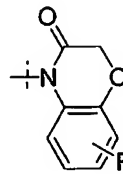
REACTION SCHEME 12

[061] The piperidine of Formula (A2), in which R⁸ and R⁹ are H or a lower alkyl group as described above can be prepared according to Reaction Scheme 13. Thus, a heteroketoester (XXX) is converted to an enol ether (XXXI), which can be coupled with an aryl boronic acid (in which aryl is phenyl or pyridyl) to provide a compound of Formula (XXXII). Reduction and hydrolysis, followed by coupling with a primary or secondary amine provides a compound of Formula (XXXV). Finally, deprotection provides the intermediate of Formula (A2). The carbonyl group of Formula (XXXIII) can be also reduced to the alcohol of Formula (XXXVI), and finally deprotection provides the intermediate of Formula (A3).

[062]

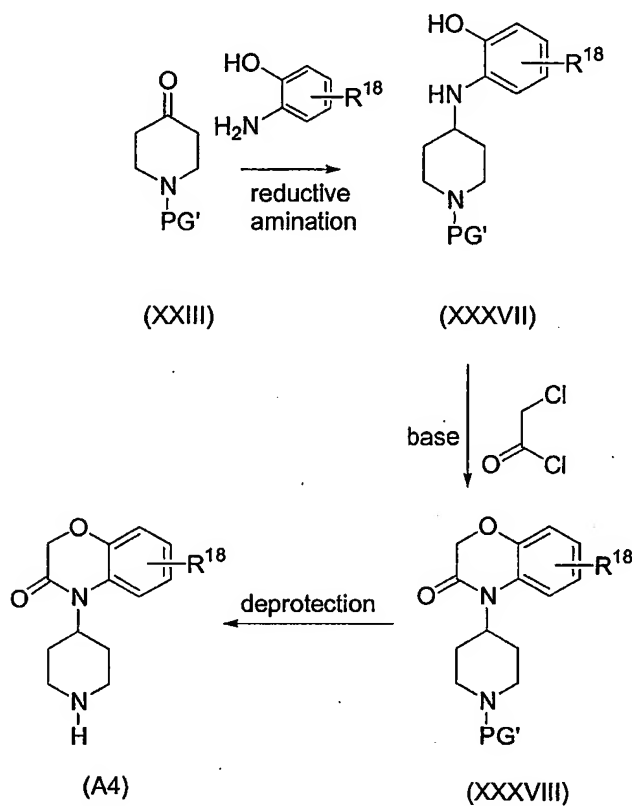
REACTION SCHEME 13



[063] Piperidines of structure (A4) in which R^{15} is , and R^{18} is as defined above can be prepared according to Reaction Scheme 14. The compound of Formula (XXXVII) can be

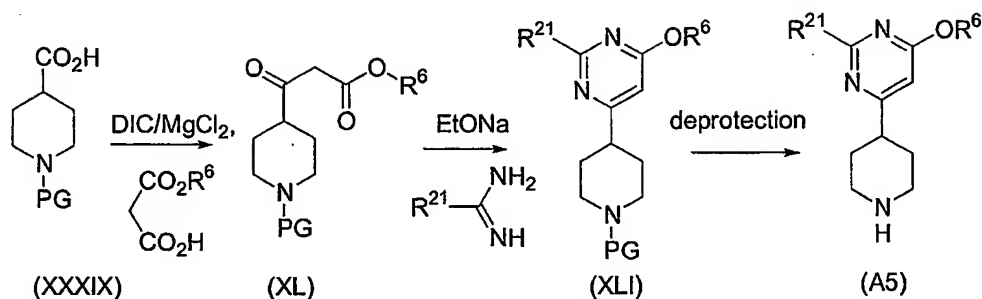
obtained under reductive amination conditions and then reacted with an acyl chloride to provide the compound of Formula (XXXVIII). Deprotection of (XXXVIII) provides intermediate (A4).

[064]

REACTION SCHEME 14

[065] Piperidines of Formula (A5), in which R¹⁵ is optionally substituted pyrimidyl, can be prepared by Reaction Scheme 15. Thus, condensation of a malonate with a carboxylic acid (XXXIX) provides β -ketone esters of Formula (XL) which is then treated with an amidine and deprotected to provide (A5).

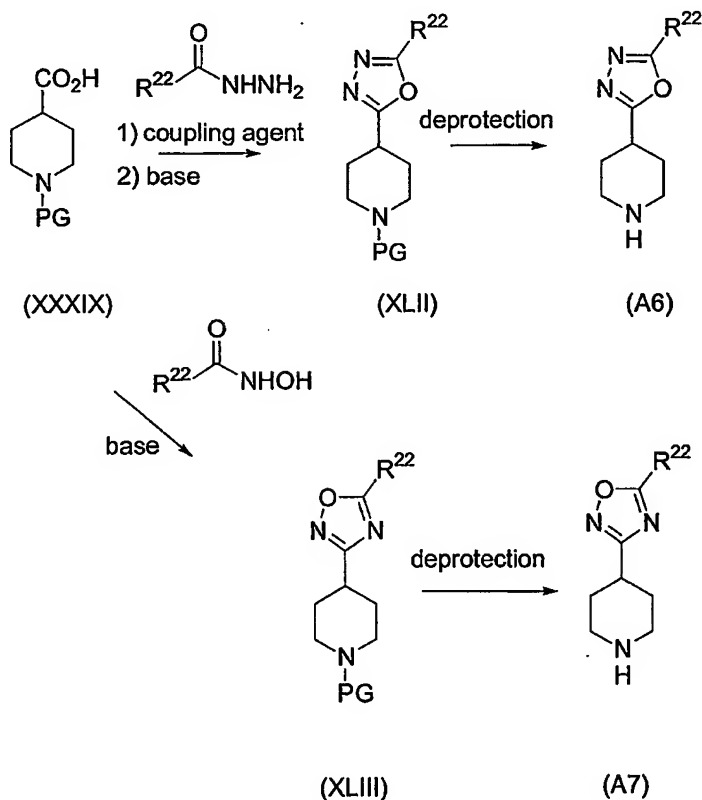
[066]

REACTION SCHEME 15

R²¹ = H, (C₁-C₆)alkyl, phenyl or pyridyl

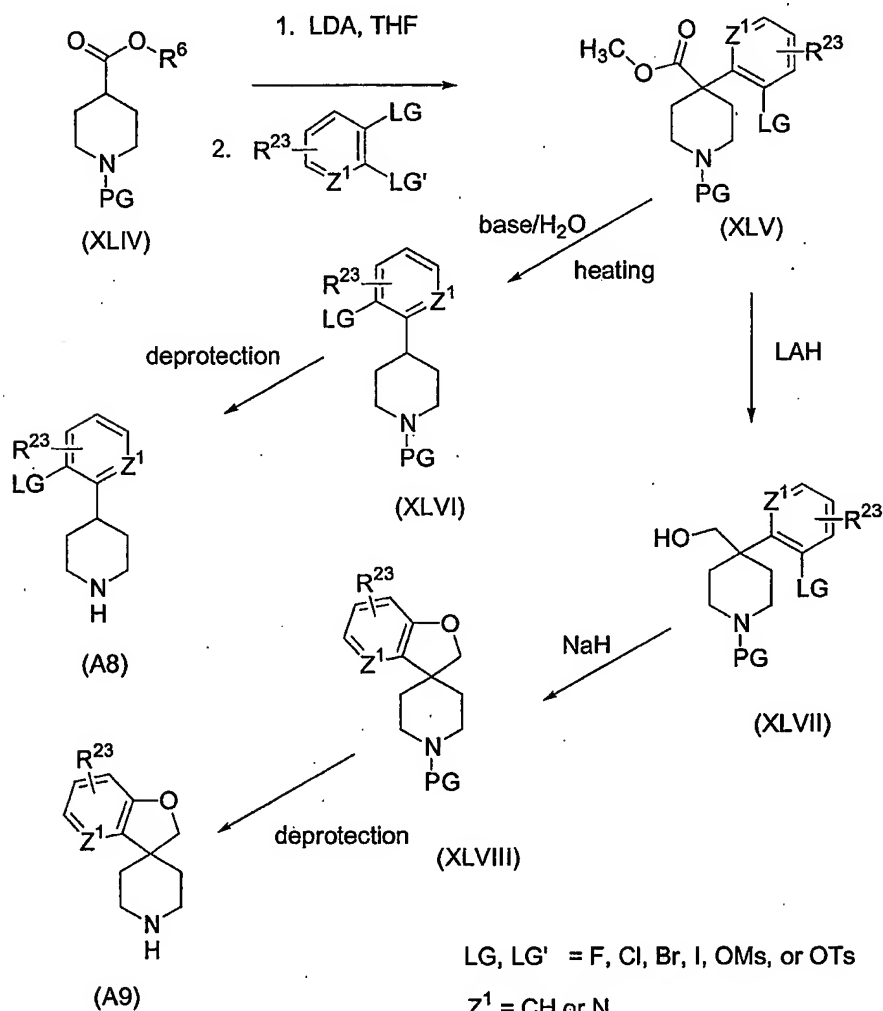
[067] Piperidine (A6), in which R¹⁵ is substituted oxadiazolyl (i.e., R²² is a alkyl group or aryl) can be prepared according to Reaction Scheme 16. The acid of Formula (XXXIX) is coupled with a hydrazide to provide an oxadiazole of Formula (XLII), which is deprotected to give (A6). By using an *N*-hydroxyamide, (A7) may also be prepared from (XXXIX) in similar fashion.

[068]

REACTION SCHEME 16

[069] Piperidines of Formula (A8) in which Z^1 is either carbon or nitrogen, and R^{23} is as defined below, can be prepared as described in Reaction Scheme 17. The compound of Formula (XLIV) is treated with an aromatic halide in basic conditions to provide the compound of Formula (XLV), which is then hydrolyzed, decarboxylated, and deprotected to provide (A8). Ester of Formula (XLV) may also be reduced with a reducing agent such as $LiAlH_4$, to provide (XLVII), which is cyclized under basic conditions and deprotection to provide the compound of Formula (A9).

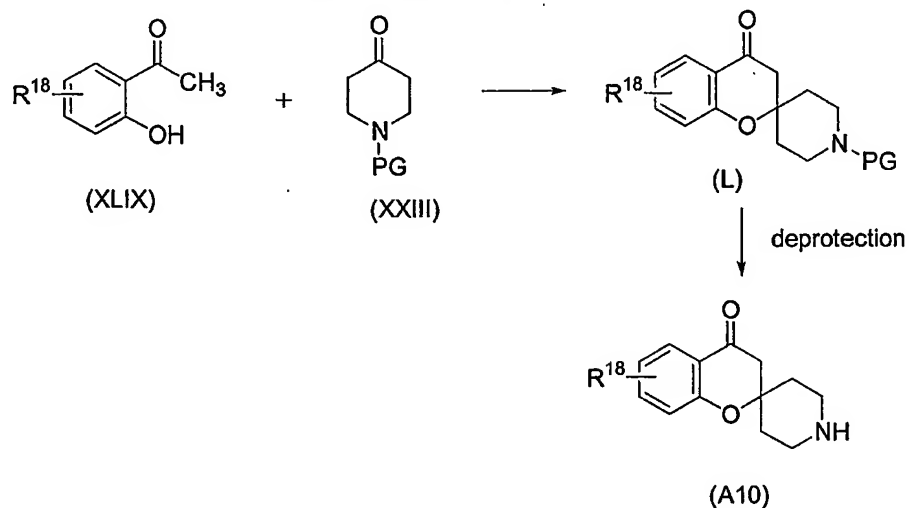
[070]

REACTION SCHEME 17

[071] The piperidine of Formula (A10), can be prepared as shown in Reaction Scheme 18. Thus, ketophenol (XLIX) is allowed to react with a ketone piperidine (XXIII) to give a pyranone of Formula (L); and deprotection of (L) gives (A10).

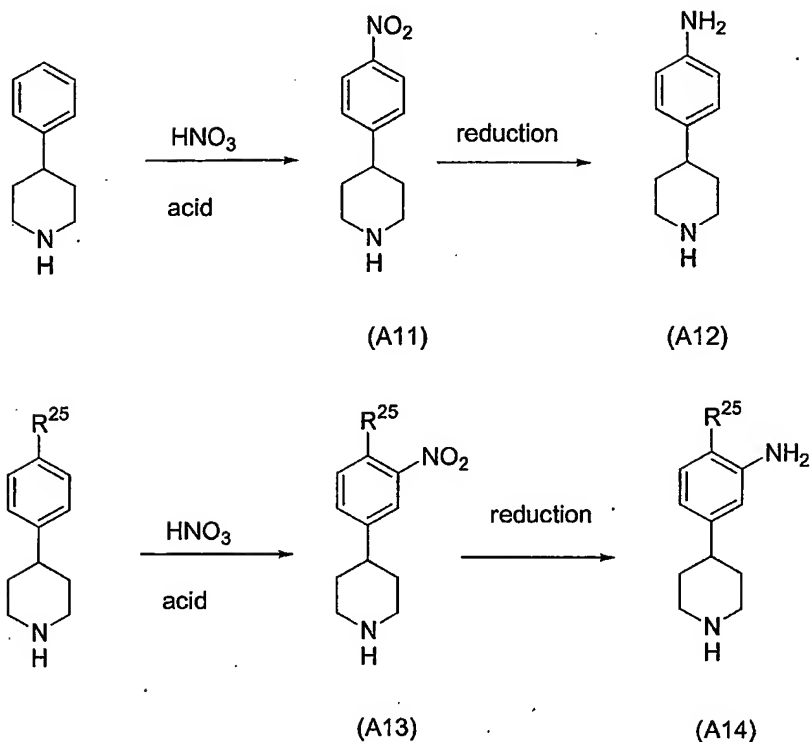
[072]

REACTION SCHEME 18



[073] Other piperidine intermediates (A11) to (A14), where R^{25} is as defined below, can be prepared as described in Reaction Scheme 19. The direct nitration of 4-phenyl piperidine, followed by reduction of the NO_2 group gives the aminophenyl compound of Formula (A12). Similarly, phenylpiperidines substituted at the 4-position can be nitrated to give the nitro substituted compound (A13); reduction of (A13) gives the amino substituted compounds of Formula (A14).

[074]

REACTION SCHEME 19

R^{25} = halo, CO_2R^5 , NHCOR^6 , CONR^8R^9 , $(\text{C}_1\text{-C}_6)\text{alkyl}$,
 $(\text{C}_1\text{-C}_6)\text{alkoxy}$, NH_2 , NO_2 , CN , and CF_3

[075] The present invention is further illustrated by the following examples which should not be construed as limiting in any way. The contents of all cited references (including literature references, issued patents, published patent applications as cited throughout this application) are hereby expressly incorporated by reference.

ABBREVIATIONS AND ACRONYMS

[076] When the following abbreviations are used herein, they have the following meaning:

Ac_2O	acetic anhydride
anhyd	anhydrous
aq	aqueous
BH_3	borane
Bn	benzyl
BOC	<i>tert</i> -butoxycarbonyl
BTMAICl_2	benzyltrimethylammonium dichloriodate

<i>n</i> -BuLi	<i>n</i> -butyllithium
<i>t</i> -BuLi	<i>t</i> -butyllithium
Cbz	benzyloxycarbonyl
CDI	carbonyldiimidazole
Celite®	diatomaceous earth filter agent, ® Celite Corp.
CI-MS	chemical ionization mass spectroscopy
mCPBA	3-chloroperoxybenzoic acid
DAST	(diethylamino)sulfur trifluoride
DCE	1,2-dichloroethane
DCM	dichloromethane
DIEA	diisopropylethylamine
DMAP	4-dimethylaminopyridine
DME	dimethoxyethane
DMF	<i>N,N</i> -dimethylformamide
DMSO	dimethylsulfoxide
EDCI	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
equiv	equivalent(s)
EtOAc	ethyl acetate
EtOH	ethanol (100%)
Et ₂ O	diethyl ether
Et ₃ N	triethylamine
h	hour(s)
HPLC-MS	high performance liquid chromatography- mass spectroscopy
HOBT	1-hydroxybenzotriazole hydrate
KO ^{<i>t</i>} Bu	potassium <i>tert</i> -butoxide
LDA	lithium diisopropylamide
LiAlH ₄	lithium aluminum hydride
LiBH ₄	lithium borohydride
LiHMDS	lithium bis(trimethylsilyl)amide
MeOH	methanol
NaBH ₄	sodium borohydride
Na(OAc) ₃ BH	sodium triacetoxyborohydride
NMM	4-methylmorpholine
Pd •(dppf)Cl ₂	[1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)
Pd(PPh ₃) ₄	tetrakis(triphenylphosphine)palladium(0)
Pd(OAc) ₂	palladium acetate

RT	HPLC retention Time
R _f	TLC retention factor
rt	room temperature
TBDMS	<i>tert</i> -butyldimethylsilyl
TBDMSCl	<i>tert</i> -butyldimethylsilyl chloride
TBDMSOTf	<i>tert</i> -butyldimethylsilyl trifluoromethanesulfonate
TEA	triethylamine
THF	tetrahydrofuran
TFA	trifluoroacetic acid
TLC	thin layer chromatography
Tf	trifluoromethanesulfonyl

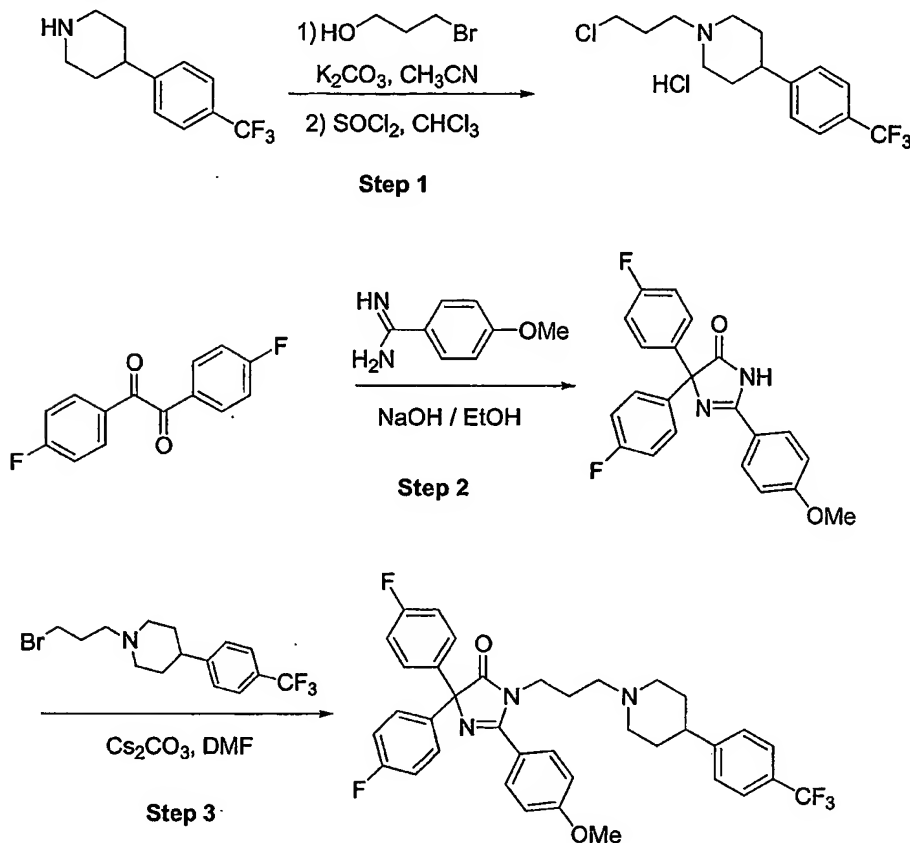
GENERAL EXPERIMENTAL PROCEDURES

[077] HPLC-electrospray mass spectra (HPLC ES-MS) were obtained using a Hewlett-Packard 1100 HPLC equipped with a quaternary pump, a variable wavelength detector, a YMC Pro C18 2.0 mm x 23 mm column, and a Finnigan LCQ ion trap mass spectrometer with electrospray ionization. Gradient elution from 90% A to 95% B over 4 minutes was used on the HPLC. Buffer A was 98% water, 2% acetonitrile, and 0.02% TFA; and Buffer B was 98% acetonitrile, 2% water, and 0.018% TFA. Spectra were scanned from 140-1200 amu using a variable ion time according to the number of ions in the source.

[078] Proton (¹H) nuclear magnetic resonance (NMR) spectra were measured with a General Electric GN-Omega 300 (300 MHz) spectrometer with either Me₄Si (δ 0.00) or residual protonated solvent (CHCl₃ δ 7.26; MeOH δ 3.30; DMSO δ 2.49) as standard. Carbon (¹³C) NMR spectra were measured with a General Electric GN-Omega 300 (75 MHz) spectrometer with solvent (CDCl₃ δ 77.0; d₃-MeOD; δ 49.0; d₆-DMSO δ 39.5) as standard.

[079] Chiral separations were performed using a commercially available Chiracel® AD HPLC column, eluting with a gradient of isopropanol in hexane (from 1% to 15%) with addition of 0.1% trifluoroacetic acid.

[080]

EXAMPLE 1**Preparation of 5,5-bis(4-fluorophenyl)-2-(4-methoxyphenyl)-3-(3-[4-[4-(trifluoromethyl)phenyl]-1-piperidinyl]propyl)-3,5-dihydro-4H-imidazol-4-one****[081] Step 1. Preparation of 1-(3-chloropropyl)-4-[4-(trifluoromethyl)phenyl]piperidine**

A 100 mL round bottomed flask was charged with K_2CO_3 (9.1 g, 65.4 mmol) and 4-(4-trifluorophenyl)-piperidine (3 g, 13.1 mmol). CH_3CN (50 mL) followed by 3-bromopropanol (1.36 mL, 15.0 mmol) were added to the solids. The reaction was allowed to stir at 23°C for 16 h. The reaction mixture was filtered through a plug of Celite® and concentrated *in vacuo*. The resulting yellow/orange oil solidified over 2 h under high vacuum to provide 1-(3-hydroxy)-4-[4-(trifluoromethyl)phenyl]piperidine, which was used directly in the next without further purification.

[082] The above alcohol was dissolved in $CHCl_3$ (10 mL), thionyl chloride (9.5 mL, 130.8 mmol) was added, and the reaction was capped with a plastic cap. The reaction did produce a small amount of bubbling and the cap was vented once. The reaction was allowed to stir for 12 h at which point TLC analysis indicated the reaction had gone to completion. The reaction mixture was concentrated *in vacuo* to provide 1-(3-chloropropyl)-4-[4-(trifluoromethyl)phenyl]piperidine

as a white solid (4.21 g, 94 % yield). LC-MS RT = 2.06 min (M + H)⁺ 306.1 calc'd for C₁₅H₂₀F₃NCl, found 306.4.

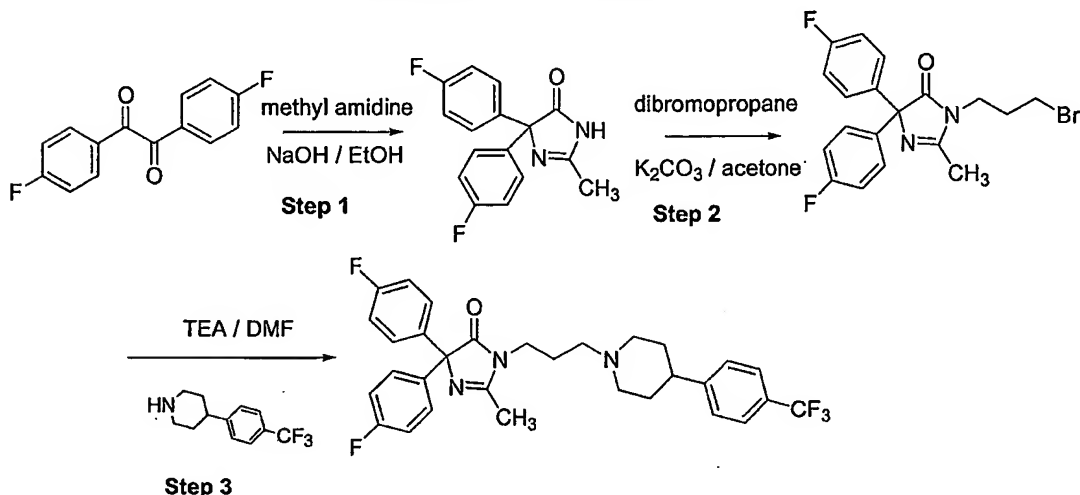
[083] Step 2. Preparation of 5,5-bis(4-fluorophenyl)-2-(4-methoxyphenyl)-3,5-dihydro-4H-imidazol-4-one

A 50 mL round bottomed flask was charged with 4-methoxy-benzamidine (500 mg, 3.33 mmol) and difluorobenzil (820 mg, 3.33 mmol). The solids were dissolved in EtOH (20 mL) and a 2 N aq solution of NaOH (5 mL) was added. The reaction flask was fitted with a condenser and heated to 80°C for 8 h. The reaction mixture was cooled to 23°C and then concentrated *in vacuo*. The remaining solid was diluted with EtOAc (100 mL), washed with H₂O (2 x 20 mL), and brine (15 mL). The organic layer was dried over Na₂SO₄ and concentrated *in vacuo*. The crude oil was purified by flash column chromatography [(35 g silica gel) 4:1 Hex:EtOAc] to provide the desired product (943.8 mg, 75% yield) as a white powder. ¹H NMR (300 MHz, CD₃OD): δ 10.20 (s, br, 1H), 8.00 (m, 2H), 7.57 (m, 3H), 7.23 (m, 2H), 6.95 (m, 6H), 3.80 (s, 3H); LC-MS RT = 3.04 min (M + H)⁺ 379.1 calc'd for C₂₂H₁₇F₂N₂O₂, found 379.2.

[084] Step 3. Preparation of 5,5-bis(4-fluorophenyl)-2-(4-methoxyphenyl)-3-(3-{4-(trifluoromethyl)phenyl}-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one

The chloride from Step 1 (50.0 mg, 0.132 mmol) and imidazalone from Step 2 (60.6 mg, 0.198 mmol) were mixed in DMF (1.5 mL) with Cs₂CO₃ (129 mg, 0.396 mmol). The reaction was allowed to stir 16 h at rt and TLC analysis indicated that the reaction had gone to completion. The mixture was filtered through a plug of cotton and washed with CH₃CN. The filtrate was filtered a second time through a nylon frit and purified by HPLC [CH₃CN: H₂O (0.1% TFA)] to provide the product (50.2 mg, 50% yield) as a white solid. ¹H NMR (300 MHz, CD₃OD): δ 7.79 (m, 2H), 7.62 (m, 2H), 7.50 (m, 4H), 7.42 (m, 2H), 7.16 (m, 6H), 3.91 (s, 3H), 3.80 (m, 2H), 3.55 (m, 2H), 3.11-2.89 (m, 5H), 2.18-1.84 (m, 6H); LC-MS RT = 2.92 min (M + H)⁺ 648.3 calc'd for C₃₇H₃₅F₅N₃O₂, found 648.5.

[085]

EXAMPLE 2**5,5-bis(4-fluorophenyl)-2-methyl-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one****[086] Step 1. Preparation of 5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one**

A mixture of difluorobenzil (492 mg, 2 mmol), acetamidine hydrochloride (189 mg, 2 mmol), NaOH (1 M aq solution, 5 mL) in 25 mL ethanol was heated at 100°C in a sealed vial for 1 h. The solution was evaporated to remove most solvent, and the residue was treated with excess saturated ammonium chloride. The solution was extracted with EtOAc (3x). The extracts were combined, washed with water and brine, dried over MgSO₄, and evaporated to afford pure desired product (556 mg, 97%). (C₁₆H₁₂F₂N₂O) LC-MS, RT 2.08 min., M + H 287; ¹H NMR (CD₂Cl₂) 7.9 (s, 1H), 7.3 (m, 4H), 6.9 (m, 4H), 2.2 (s, 3H)

[087] Step 2. Preparation of 3-(3-bromopropyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

The imidazolone derivative from Step 1 (680 mg, 2 mmol), 1,3-dibromopropane (2.01 g, 10 mmol), and cesium carbonate (1.3 g, 4 mmol) were mixed with anhyd DMF, and the mixture stirred at rt for 12 h, followed by treatment with cold water to form a solution which was extracted by ethyl acetate (3x). The extracts were combined, washed with water and brine, dried over MgSO₄, and evaporated to dryness. The residue was separated by column (15% EtOAc in hexane) to give desired product (745 mg, 91%). (C₁₉H₁₇BrF₂N₂O) LC-MS M+H 407.

[088] Step 3. Preparation of 5,5-bis(4-fluorophenyl)-2-methyl-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one

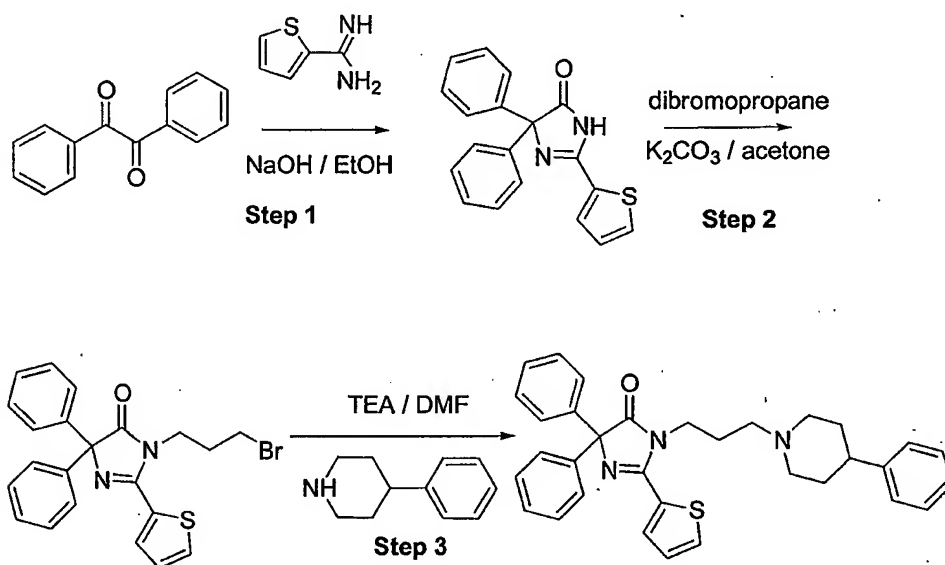
The imidazolone derivative from Step 2 (81.4 mg, 0.2 mmol), 4-(4-trifluoromethylphenyl)piperidine hydrochloride, and triethylamine (90.9 mg, 0.9 mmol) in anhyd methylene chloride

(2.5 mL) were stirred at rt for 72 h. The solution was directly separated by preparative TLC (5% hexane in EtOAc) to furnish pure desired product (26 mg, 23%). ($C_{31}H_{30}F_5N_3O$) LC-MS, RT 2.4 min., M+H 556; 1H NMR (300 MHz, CD_2Cl_2): δ 1.4 (m, 2H), 1.6 (m, 4H), 1.8 (m, 2H), 2.1 (m, 2H), 2.2 (s, 3H), 2.3 (m, 1H), 3.5 (m, 2H), 6.9 (m, 4H), 7.1 (m, 2H), 7.2 (m, 2H), 7.4 (m, 4H).

[089]

EXAMPLE 3

Preparation of 5,5-Diphenyl-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one



[090] Step 1. Preparation of 5,5-Diphenyl-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one

To an ethanol (20 mL) solution of benzil (2 g, 10 mmol, 1 equiv) in a sealed tube (250 mL) were added aq sodium hydroxide (1 g in 5 mL, 25 mmol, 2.5 equiv) and 2-amidinothiophene (1 g, 8 mmol, 0.8 equiv). The tube was sealed and heated to 100°C for 3 h with magnetic stirring. The resulting solution was concentrated *in vacuo*. Ethyl acetate (30 mL) extraction of the product from the aqueous layer, drying over sodium sulfate, and concentration yielded desired product (2.5 g, 90% yield), which was used for the next step without further purification.

[091] Step 2. Preparation of 3-(3-bromopropyl)-5,5-diphenyl-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one

To an acetone (20 mL) solution of the product of Step 1 (2.5 g, 8 mmol, 1 equiv) was added 1,3-dibromopropane (10 mL) and potassium carbonate (5 g). The resulting mixture was refluxed for 2 h then filtered to remove solids. The filtrate was concentrated *in vacuo*, and the residue was purified by silica gel chromatography (hexanes/ethyl acetate) to yield desired product (1.3 g, 40% yield).

yield). ($C_{22}H_{19}BrN_2OS$) LC-MS, RT 3.65 min., M+H 439.2; 1H NMR (CD_2Cl_2): δ 2.20 (m, 2H), 3.40 (t, 2H), 4.00 (t, 2H), 7.20 (m, 1H), 7.30 (m, 6H), 7.40 (m, 4H), 7.50 (d, 1H), 7.60 (d, 1H).

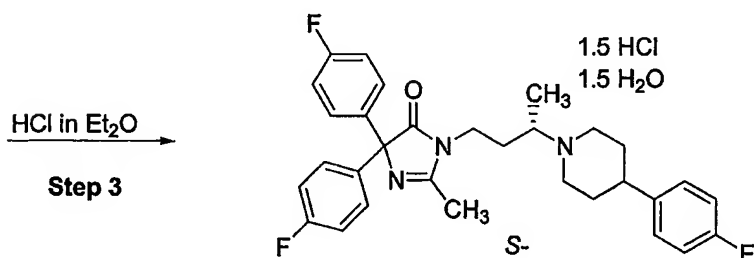
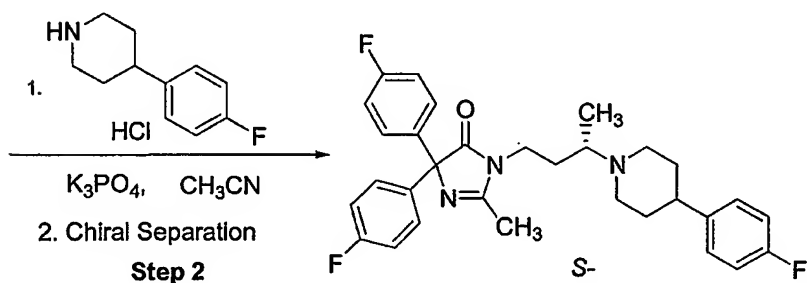
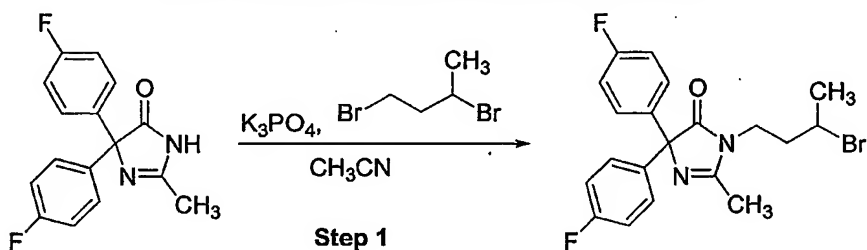
[092] Step 3. Preparation of 5,5-Diphenyl-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one

To a DMF (1 mL) solution of bromide from Step 2 (50 mg, 0.11 mmol) was added triethylamine (0.2 mL) and 4-phenyl piperidine (50 mg, 0.31 mmol). The mixture was stirred for 16 h at rt. Ethyl acetate (2 mL) was added to the solution, and the mixture was washed with brine (5 mL). The ethyl acetate solution was concentrated, and the residue was purified by HPLC to yield the TFA salt of the desired product (34 mg, 20% yield). ($C_{33}H_{33}N_3OS$) LC-MS, RT 2.71 min., M+H, 520.2; 1H NMR (CD_2Cl_2): δ 1.90 (m, 2H), 2.20 (m, 4H), 2.60 (m, 3H), 3.00 (t, 2H), 3.60 (dd, 2H), 4.00 (t, 2H), 7.20 (m, 5H), 7.35 (m, 7H), 7.55 (m, 4H), 7.70 (d, 1H), 7.75 (d, 1H), 13.00 (s, 1H).

[093]

EXAMPLE 4

Preparation of (+) or (-)- 5,5-Bis-(4-fluoro-phenyl)-3-[3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-butyl]-2-methyl-3,5-dihydro-4H-imidazol-4-one



[094] Step 1. Preparation of 3-(3-bromobutyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

To a solution of the 5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one (5.00 g, 17.47 mmol) in CH₃CN (100 mL) was added K₃PO₄ (18.54 g, 87.33 mmol). To the resulting slurry was added 1,3-dibromobutane (5.27 mL, 43.66 mmol), and the reaction was allowed to stir for 16 h. The slurry was filtered through a glass frit and the filtrate was concentrated *in vacuo*. The resulting paste was dissolved in EtOAc and purified by flash column chromatography [(200 g silica gel) 3:1 Hex:EtOAc, 1:1 Hex:EtOAc then 3:1 Hex:EtOAc with 5% MeOH] to provide the product (6.22 g, 84.5% yield) as a pale yellow solid. LC-MS RT = 3.25 min (M + H)⁺ 421.1 calc'd for C₂₀H₂₀BrF₂N₂O, found 421.1.

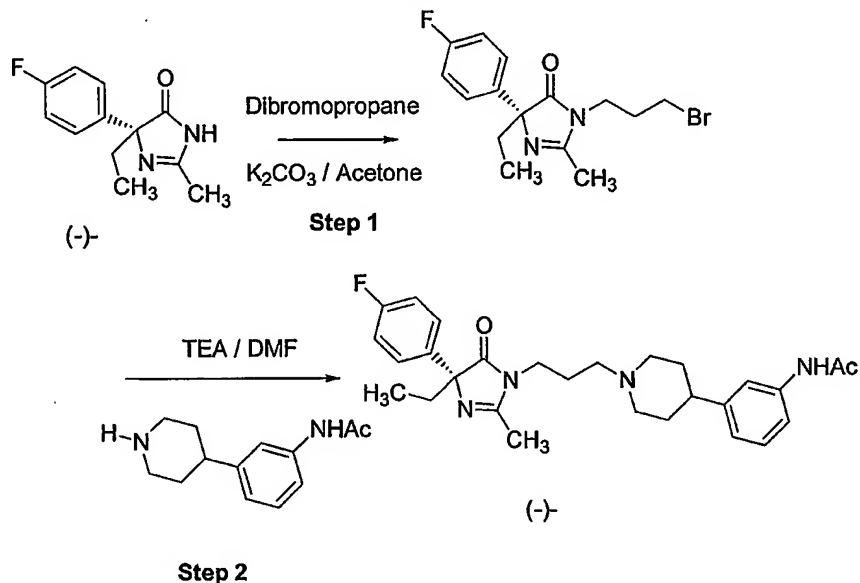
[095] Step 2. Preparation of (S)-5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one

To a solution of the alkyl bromide from Step 1 (4.34 g, 10.30 mmol) in CH₃CN (100 mL) was added K₃PO₄ (10.93 g, 51.51 mmol). To the resulting slurry was added the piperidine hydrochloride (3.33 g, 15.45 mmol), and the reaction mixture was allowed to stir for 4 days. An additional piperidine hydrochloride (1 g, 4.6 mmol) was added. The reaction was allowed to stir for another 3 days. The mixture was filtered through a glass frit and the filtrate was concentrated *in vacuo*. The resulting paste was dissolved in EtOAc and was purified by flash column chromatography [(200 g silica gel) 3:1 Hex:EtOAc, 1:1 Hex:EtOAc, then 3:1 Hex:EtOAc 10% MeOH] to provide a pale yellow oil (3.84 g 72% yield). The yellow oil was purified by chiral column HPLC. Isolation of the pure desired enantiomer provided (S)-isomer (850 mg), as a clear glass. ¹H NMR (CD₃OD): δ 7.58-7.44 (m, 5H), 7.38-7.21 (m, 2H), 7.18-7.01 (m, 5H), 3.98 (m, 2H) 3.44 (m, 1H), 3.39-3.15 (m, 6H), 2.90 (m, 1H), 2.50 (m, 1H), 2.20-2.00 (m, 6H), 1.45 (d, J = 6.7 Hz, 3H); LC-MS RT = 2.49 min (M + H)⁺ 520.3 calcd for C₃₁H₃₃F₃N₃O found 520.2. [α]_D^{24.5} = + 22.3° (c = 1.2, EtOH).

[096] Step 3. Preparation of HCl salt of (S)-5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one

The glass from Step 2 was dissolved in Et₂O and a 2 N HCl in ether solution was added dropwise. Instantly, a white precipitate formed. That precipitate was isolated by vacuum filtration and dried under reduced pressure to provide the product (686 mg, 69%, C₃₁H₃₂F₃N₃O · 1.5HCl · 1.5H₂O).

[097]

EXAMPLE 5**Preparation of (-)- or (+)-N-[3-(1-{3-[(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide****[098] Step 1. 3-(3-bromopropyl)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one**

(-)-5-Ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one (0.22 g, 1.02 mmol, prepared according to **Example 8**, was dissolved in anhyd DMF (5 mL) followed by the addition of solid cesium carbonate (0.66 g, 2.04 mmol). 1,3-Dibromopropane (1.03 g, 5.09 mmol) was added dropwise to the reaction mixture via syringe and was allowed to stir at rt for 18 h. The reaction was then quenched with water, and extracted with ethyl acetate (2 x 30 mL). The combined organic layers were then dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude reaction mixture was then purified by flash chromatography (20% ethyl acetate / hexane) to yield a pale yellow oil (0.22 g, 63%). ($C_{15}H_{18}BrFN_2O$) LC-MS, RT 2.45 min., M+H 341.5, 343.1; R_f 0.27 (1:1 EtOAc / Hex).

[099] Step 2. Preparation of (-)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3-(3-{4-[3-(acetamino)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one

N-[3-(4-piperidinyl)phenyl]acetamide (0.08 g, 0.32 mmol) was dissolved in anhyd DMF (3 mL) followed by the dropwise addition of triethylamine (0.14 g, 0.81 mmol). 3-(3-Bromopropyl)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one from Step 1 (0.11 g, 0.32 mmol) was then added to the reaction which was then heated to 80°C for 18 h. The reaction was quenched with water and extracted with ethyl acetate (2 x 30 mL). The combined organic layer

was then washed with saturated NaCl and dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude compound was purified by flash chromatography (4% MeOH, 1% NH_4OH , 95% CHCl_3) to yield the title compound as a yellow oil (0.06g, 37%). ($\text{C}_{28}\text{H}_{35}\text{FN}_4\text{O}$) LC-MS, RT 1.98 min., $\text{M}+\text{H}$ 479.2 ^1H NMR (DMSO) δ 0.70 (m, 3H), 1.5 (m, 2H), 1.6 (m, 3H), 1.8 (m, 4H), 2.0 (s, 3H), 2.2 (m, 2H), 2.3 (s, 3H), 2.4 (m, 1H), 2.8 (m, 3H), 3.5 (m, 2H), 6.9 (m, 1H), 7.1 (m, 3H), 7.3 (m, 1H), 7.4 (m, 1H), 7.5 (m, 2H), 9.8 (s, 1H); R_f 0.2 (4% MeOH, 1% NH_4OH , 95% CHCl_3). $[\alpha]_D -17.7$ ($c = 0.33$, CHCl_3).

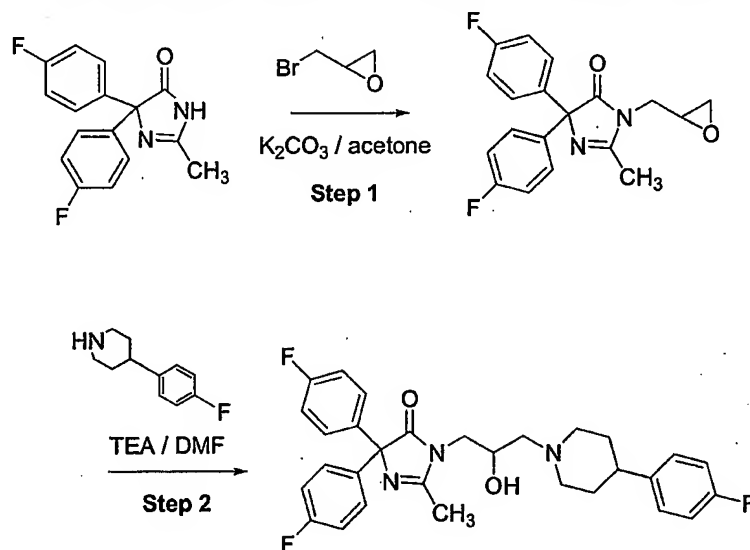
[100] Preparation of (+)-N-[3-(1-[3-[(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide:

By using (+)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one (0.22 g, 1.02 mmol), the title compound was obtained by the similar procedure (0.04 g, 25%). $[\alpha]_D +33.9$ ($c = 0.33$, CHCl_3).

[101]

EXAMPLE 6

Preparation of 5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]-2-hydroxypropyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one



[102] Step1. Preparation of 5,5-bis(4-fluorophenyl)-2-methyl-3-(2-oxiran-2-ylmethyl)-3,5-dihydro-4H-imidazol-4-one:

The imidazolone derivative from Step 1 of Example 2 (1.15g, 4 mmol), epibromohydrin (610 mg, 4.4 mmol), and cesium carbonate (2.5g, 8 mmol) were mixed with anhyd DMF (15 mL). The mixture was stirred at rt overnight. The solvent was then removed by evaporation, and the residue

was separated by flash column chromatography (15% EtOAc in hexane) to afford desired product (1.05 g, 77%). ($C_{19}H_{16}F_2N_2O_2$) LC-MS, M+H 343.

[103] Step 2. Preparation of 5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]-2-hydroxypropyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one

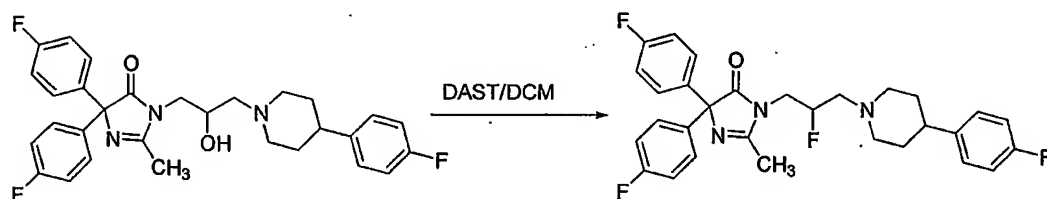
The imidazolone derivative from Step 1 (68.6 mg, 0.2 mmol), 4-(4-fluorophenyl)piperidine hydrochloride, cesium carbonate (160 mg, 0.5 mmol), and sodium iodide (catalytic amount) in anhyd DMF (2 mL) were heated at 100°C for 24 h. The mixture was directly purified by preparative TLC (5% MeOH in DCM) to furnish pure desired product (61.6 mg, 59%).

($C_{30}H_{30}F_3N_3O_2$) LC-MS, RT 2.26 min., M+H 522; 1H NMR (CD_2Cl_2) δ 1.6 (m, 4H), 2.4 (m, 3H), 2.4 (m, 2H), 2.8 (m, 2H), 3.0 (m, 1H), 3.4 (m, 2H), 3.7 (m, 2H), 3.9 (m, 1H), 7.0 (m, 6H), 7.2 (m, 2H), 7.5 (m, 4H), 8.0 (s, 1H).

[104]

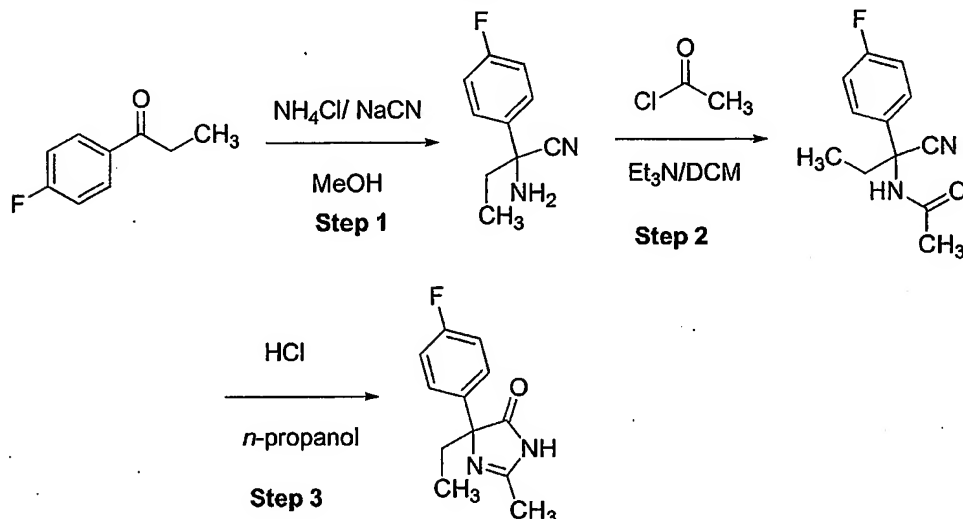
EXAMPLE 7

Preparation of 3-{2-fluoro-3-[4-(4-fluorophenyl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one



[105] To a solution of 5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]-2-hydroxypropyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one from **Example 6** (83.4 mg, 0.2 mmol) in DCM (2 mL), was added DAST (36 mg, 0.22 mmol), and the solution was stirred at rt for 5 h, followed by treatment with cold water. The organic layer was separated, dried, and evaporated. The residue was then separated by column (MeOH:EtOAc:hexane 5:20:75) to afford pure desired product (60.2 mg, 57%). ($C_{30}H_{29}F_4N_3O$) LC-MS RT 2.78 min., M+H 524; 1H NMR (CD_2Cl_2) δ 1.8 (m, 4H), 2.2 (m, 2H), 2.4 (s, 3H), 2.5 (m, 1H), 2.6 (m, 4H), 3.0 (m, 2H), 4.8 (m, 1H), 7.0 (m, 6H), 7.2 (m, 2H), 7.5 (m, 4H).

[106]

EXAMPLE 8**Preparation and chiral resolution of 5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one****[107] Step 1. Preparation of 2-Amino-2-(4-fluorophenyl)butanenitrile**

To a solution of 4-fluorophenylpropanone (10.0 g, 65.72 mmol) in methanol (50 mL) was added a suspension of sodium cyanide (3.30 g, 67.33 mmol) and ammonium chloride (4.00 g, 74.78 mmol) in a sealed tube. The reaction mixture was stirred for 15 minutes at rt then warmed to 60°C for 24 h. After 24 h, the reaction mixture was cooled to rt, and 1 mL water was added to the reaction. The resulting reaction mixture was stirred for an additional 48 h. Water (50 mL) was added and the mixture was extracted with ethyl acetate (2 x 50 mL). The ethyl acetate extract was washed with saturated sodium bicarbonate (50 mL), dried over MgSO_4 , filtered to remove solids, and concentrated *in vacuo*. The crude product was then purified by flash chromatography (15-25% ethyl acetate / hexane) to yield a white crystalline solid (8.0 g, 68%): $^1\text{H NMR}$ (CDCl_3) δ 0.95 (t, $J = 7.5$ Hz, 3H), 1.90 (m, 2H), 2.10 (s, 2H), 7.00 (t, $J = 6$ Hz, 2H), 7.60 (m, 2H); R_f : 0.5 (1:1 EtOAc/ Hex).

[108] Step 2. Preparation of N-[1-cyano-1-(4-fluorophenyl)propyl]acetamide

To a solution of 2-amino-2-(4-fluorophenyl)butanenitrile (2.76 g, 15.49 mmol) in dichloromethane (25 mL) was added triethylamine (2.38 mL, 17.04 mmol) followed by the dropwise addition of acetyl chloride (1.34 g, 17.04 mmol) at rt. The reaction mixture was stirred for 4 h and quenched with water (50 mL), then extracted with dichloromethane (2 x 30 mL). The organic layers were combined and washed with saturated NaCl (50 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo* to afford the desired compound as a white crystalline solid (3.10 g, 91%): ($\text{C}_{12}\text{H}_{13}\text{FN}_2\text{O}$)

LC-MS, RT 2.48 min., M+H 220.8; ^1H NMR (CDCl_3) δ 0.95 (t, $J = 7.5$ Hz, 3H), 1.80 (m, 1H), 1.90 (s, 3H), 2.10 (m, 1H), 7.00 (t, $J = 6$ Hz, 2H), 7.40 (m, 3H); R_f 0.2 (1:1 EtOAc / Hex).

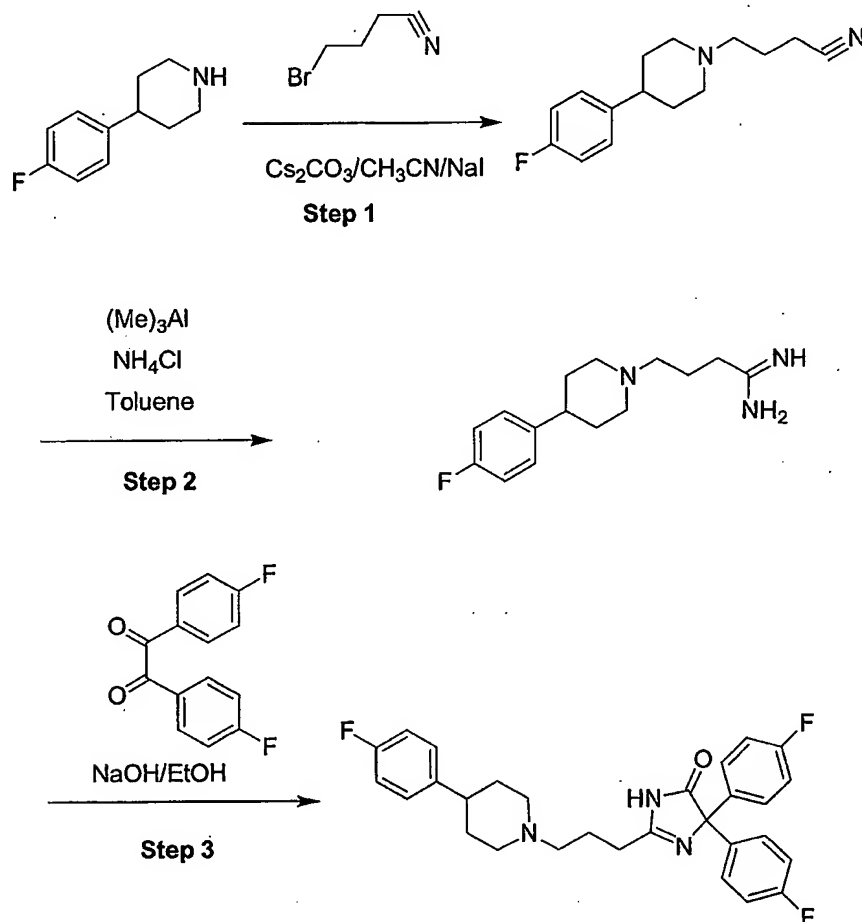
[109] Step 3. Preparation of 5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

To a solution of *N*-[1-cyano-1-(4-fluorophenyl)propyl]acetamide (3.10 g, 14.08 mmol) in *n*-propanol (30 mL) was added 4 M HCl (in dioxane) dropwise while stirring at rt. The reaction mixture was then heated to 50°C for 18 h. The reaction mixture was quenched with water (50 mL) and extracted with dichloromethane (2 x 30 mL). The organic layers were combined and washed with saturated NaCl (50 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo* to afford the desired material as a white crystalline solid (2.59 g, 84%): ($\text{C}_{12}\text{H}_{13}\text{FN}_2\text{O}$) LC-MS, RT 1.2 min., M+H 221.1; ^1H NMR (CDCl_3) δ 0.9 (t, $J = 7.5$ Hz, 3H), 2.10 (q, $J = 7.2$ Hz, $J = 14.7$ Hz, 3H), 2.60 (s, 3H), 7.30 (t, $J = 9$ Hz, 2H), 7.60 (q, $J = 9$ Hz, 2H); R_f 0.16 (1:1 EtOAc / Hex).

[110] Resolution of (+) and (-) enantiomers: (+)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one and (-)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

The (+)- and (-)- enantiomers of 5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one were separated by chiral HPLC; Column: Chiracel OD, 20 x 250 mm; Mobile Phase, hexane/isopropanol w/ 0.1% TEA; Flow Rate, 15 mL/min.; Detector (UV), 250 nm. (-)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one: retention time 10.5 min, $[\alpha]_D -92.4$ ($c=0.43$, CHCl_3). (+)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one .retention time 13.6 min, $[\alpha]_D +75.0$ ($c=0.33$, CHCl_3).

[111]

EXAMPLE 9**Preparation of 5,5-bis(4-fluorophenyl)-2-{3-[4-(4-fluorophenyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one****[112] Step 1. Preparation of 4-[4-(4-fluorophenyl)-1-piperidinyl]butanenitrile**

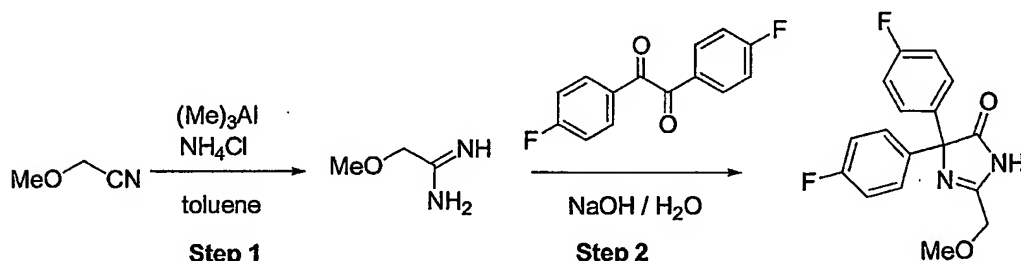
To a solution of 4-(4-fluorophenyl)piperidine hydrochloride (1 g, 4.64 mmol) in acetonitrile (50 mL) was added 4-bromobutyronitrile (0.686 g, 4.64 mmol), cesium carbonate (3.777 g, 11.59 mmol), and sodium iodide (0.174 g, 1.16 mmol). The reaction mixture was heated to 60°C with stirring for 24 h. It was cooled to rt and filtered to remove the solid. The liquid solution was extracted with ethyl acetate (3 x 50 mL), and washed with water (3 x 50 mL). The organic layer was dried over MgSO_4 , filtered, and concentrated to give the crude product (1.19 g, 100% yield) which was used in Step 2 without further purification.

[113] Step 2. Preparation of 4-[4-(4-fluorophenyl)-1-piperidinyl]butanimidamide

To a solution of ammonium chloride (0.61 g, 4.87 mmol) in toluene (5 mL) at 0°C was slowly added 2.0 M trimethylaluminum (2.44 mL, 4.87 mmol) over 15 minutes and stirred at 0°C for additional 10 minutes, and allowed to warm to rt for 30 minutes. A solution of 4-[4-(4-fluorophenyl)-1-piperidinyl]butanenitrile from Step 1 (0.4 g, 1.62 mmol) in toluene (5 mL) was added to the reaction mixture. The mixture was heated to 80°C with stirring for 36 h, cooled to rt, and poured into a 10 g silica gel/CHCl₃ slurry, filtered, and washed with 150 mL methanol, then concentrated to give 1.2 g crude product. It was washed with CH₂Cl₂ to remove the remaining starting material, concentrated, and dried to give the title compound (0.437 g, 100% yield).

[114] Step 3. Preparation of 5,5-bis(4-fluorophenyl)-2-{3-[4-(4-fluorophenyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one

To a solution of the product from Step 2 (112 mg, 0.43 mmol) in ethanol (2 mL) was added 1.0 N sodium hydroxide solution (1.02 mL). The mixture was heated to 100°C with shaking for 30 minutes. The reaction mixture was separated by HPLC to yield the TFA salt of product (7.5 mg, 3% yield). (C₂₉H₂₈F₃N₃O) LC-MS, RT 2.74 min., M+H, 492.52. ¹H NMR (CD₃OD): 1.83 (m, 2H), 2.10 (d, 2H), 2.30 (m, 2H), 2.81 (t, 2H), 2.92 (d, 1H), 3.13 (t, 2H), 3.31 (m, 2H), 3.72 (d, 2H), 7.06 (m, 6H), 7.12 (m, 2H), 7.41 (m, 4H).

[115]**EXAMPLE 10****Preparation of 5,5-bis(4-fluorophenyl)-2-(methoxymethyl)-3,5-dihydro-4H-imidazol-4-one****[116] Step 1. Preparation of Methoxyacetoamidine**

To a cooled solution (0°C) of ammonium chloride (4.52 g, 84.41 mmol) in anhyd toluene (25 mL) was slowly added a solution of 2 M trimethylaluminum (in toluene) (42.2 mL, 84.41 mmol) dropwise. After stirring at this temperature for 30 minutes, the mixture was allowed to warm to rt for an additional 1 h. Methoxyacetonitrile (1.0 g, 14.07 mmol) was then added and the reaction mixture was heated to 80°C for 18 h. The mixture was then added to a slurry of silica gel (9.0 g) in chloroform (92 mL) at 0°C and stirred for 30 minutes followed by 1 h at rt. The mixture was then filtered and washed slowly with methanol and concentrated *in vacuo*. The remaining solid was

washed with a 9:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$ solution, filtered, and the combined filtrate was concentrated *in vacuo*. GC-MS, RT 8.65 min., M+H 89, analysis confirmed the identity of the product (1.17 g, 94%) and it was used immediately for next step without further purification.

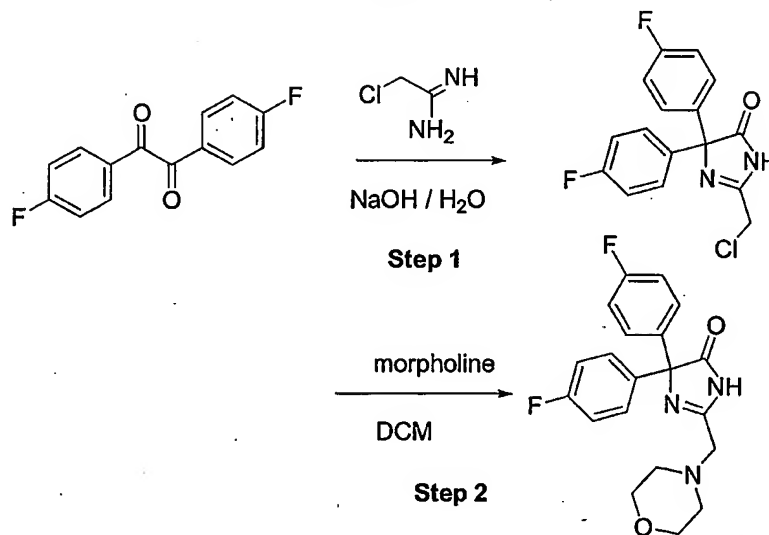
[117] Step 2. Preparation of 5,5-bis(4-fluorophenyl)-2-(methoxymethyl)-3,5-dihydro-4H-imidazol-4-one

To a solution of 4,4-difluorobenzil (2.72 g, 11.1 mmol) in ethanol (10 mL) was added the methoxyacetamidine from Step 1 (1.17 g, 13.28 mmol) and an aq solution of sodium hydroxide (1.11 g, 27 mmol) in 2.5 mL water. The reaction mixture was heated at 100°C for 2 h, then treated with water (30 mL), and extracted with ethyl acetate (2 x 30 mL). The combined organic layers were washed with saturated NaCl solution (30 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude solid was triturated with ether to yield the desired compound as a white solid (1.77 g, 51%). ($\text{C}_{17}\text{H}_{14}\text{F}_2\text{N}_2\text{O}_2$) LC-MS, RT 2.59 min., M+H 317.1; ^1H NMR ($\text{DMSO}-d_6$) δ 3.3 (s, 3H), 4.15 (s, 2H), 7.10 (m, 4H), 7.40 (m, 4H); R_f 0.49 (1:1 EtOAc / Hex).

[118]

EXAMPLE 11

Preparation of 5,5-bis(4-fluorophenyl)-2-(4-morpholinylmethyl)-3,5-dihydro-4H-imidazol-4-one



[119] Step 1. Preparation of 2-Chloromethyl-5,5-bis-(4-fluoro-phenyl)-3,5-dihydro-imidazol-4-one

To a solution of 4,4-difluorobenzil (0.50 g, 2.04 mmol) in ethanol (10 mL) was added 2-chloroacetamidine (0.32 g, 2.44 mmol) and sodium hydroxide (0.20 g, 5.09 mmol) in 2.5 mL water. The reaction mixture was then heated to 100°C for 2 h then treated with water (30 mL) and

extracted with ethyl acetate (2 x 30 mL). The combined organic layers were washed with saturated NaCl (30 mL), dried over MgSO₄ and concentrated *in vacuo*.

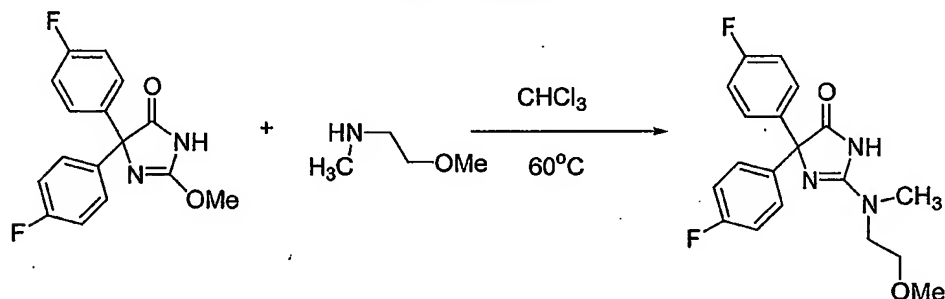
[120] Step 2. Preparation of 5,5-Bis-(4-fluoro-phenyl)-2-morpholin-4-ylmethyl-3,5-dihydro-imidazol-4-one

The crude compound was then dissolved in dichloromethane (10 mL) and treated with morpholine (0.21 g, 2.44 mmol) dropwise via syringe. The reaction allowed to stir at rt for 18 h, and concentrated *in vacuo* to yield the crude imidazolone which was used next step without further purification. (C₂₀H₁₉F₂N₃O₂) LC-MS, RT 2.27 min., M+H 372.0; R_f 0.10 (10% MeOH / CH₂Cl₂).

[121]

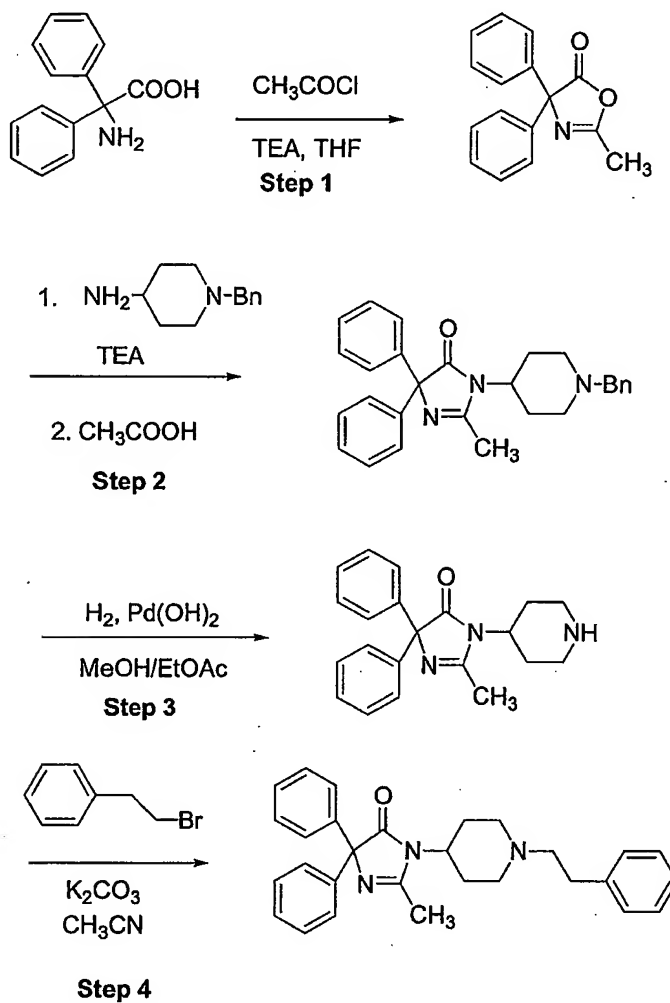
EXAMPLE 12

Preparation of 5,5-bis(4-fluorophenyl)-2-[(2-methoxyethyl)(methyl)amino]-3,5-dihydro-4H-imidazol-4-one



[122] To a solution of 5,5-bis(4-fluorophenyl)-2-methoxy-3,5-dihydro-4H-imidazol-4-one (0.15 g, 0.50 mmol, 1.0 equiv) in chloroform (3 mL) was added 2-methoxy-N-methylethanamine (0.09 g, 1.0 mmol, 2 equiv) under an argon atmosphere at rt. The reaction mixture was allowed to heat up to 60°C under argon for 18 h. The mixture was then quenched with water (2 mL) and extracted with ethyl acetate (3 x 3 mL). The combined extracts were washed with brine (5 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford a yellow oil. Purification by HPLC (0-70 acetonitrile/distilled water) yielded the desired product as colorless oil (0.1 g, 56%). (C₁₉H₁₉F₂N₃O₂) LC-MS, RT 2.86 min., M+H 360.3.

[123]

EXAMPLE 13**Preparation of 2-methyl-5,5-diphenyl-3-[1-(2-phenylethyl)-4-piperidiny]-3,5-dihydro-4H-imidazol-4-one****[124] Step 1. Preparation of 2-methyl-4,4-diphenyl-1,3-oxazol-5(4H)-one**

To a solution of amino(diphenyl)acetic acid (2.0g, 8.8 mmol, 1.0 equiv) in THF (100 mL) were added acetyl chloride (0.9 mL, 13.2 mmol, 1.5 equiv) and triethylamine (1.8 mL, 13.2 mmol, 1.5 equiv) under an argon atmosphere at rt. The reaction mixture was stirred for an additional 20 h. The mixture was then filtered through Celite[®] and washed with THF (100 mL). The filtrate was concentrated under reduced pressure to give a yellow oil. To the residue were added ethanol (100 mL) and ethyl acetate (100 mL). The white precipitate was removed by filtration and the

filtrate was concentrated under reduced pressure to yield the desired product as pale yellow solid (1.2 g, 55%). LC-MS 251.9 (M+H), RT 3.03 minutes.

[125] Step 2. Preparation of 3-(1-benzyl-4-piperidinyl)-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one

To a solution of 2-methyl-4,4-diphenyl-1,3-oxazol-5(4H)-one (1.2 g, 4.46 mmol, 1.0 equiv) in DMF (10 mL) were added 1-benzyl-4-piperidinylamine (1.4 mL, 6.68 mmol, 1.5 equiv) and triethylamine (2 mL, 14.35 mmol, 3.2 equiv) under an argon at rt. The reaction mixture was allowed to heat up at 80°C under argon atmosphere for 48 h. The mixture was then quenched with distilled water (20 mL) and extracted with ethyl acetate (3 x 15 mL). The combined extracts were washed with brine (20 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford a yellow oil. Acetic acid (8 mL) was added to the residue at rt and the mixture was heated to 110°C for 50 h. The reaction was then cooled to rt, neutralized to pH 8 with 1N sodium hydroxide, and extracted with ethyl acetate (3 x 15 mL). The combined extracts were dried over sodium sulfate, filtered, and concentrated under reduced pressure to afford a yellow solid. Purification by flash chromatography on a silica gel column (1% triethylamine/ethyl acetate) afforded the desired product as a pale yellow solid (0.9 g, 48%). LC-MS 438.3 (M+H), RT 2.36 minutes.

[126] Step 3. Preparation of 2-methyl-5,5-diphenyl-3-(4-piperidinyl)-3,5-dihydro-4H-imidazol-4-one

To a solution of 3-(1-benzyl-4-piperidinyl)-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one (0.5 g, 1.18 mmol, 1.0 equiv) in methanol (10 mL) and ethyl acetate (5 mL) were added 10% palladium hydroxide (0.45 g) and 15 drops of 4 N hydrochloric acid in 1,4-dioxane under argon atmosphere at rt. A hydrogen balloon was then attached to the top of the flask. The reaction mixture was stirred at rt for 4 h. The mixture was then filtered through Celite®, washed with ethyl acetate (50 mL) and hexanes (40 mL), and concentrated under reduced pressure to afford the desired product as a pale yellow solid (0.29 g, 74%). LC-MS 334.1 (M+H), RT 1.79 min.

[127] Step 4. Preparation of 2-methyl-5,5-diphenyl-3-[1-(2-phenylethyl)-4-piperidinyl]-3,5-dihydro-4H-imidazol-4-one

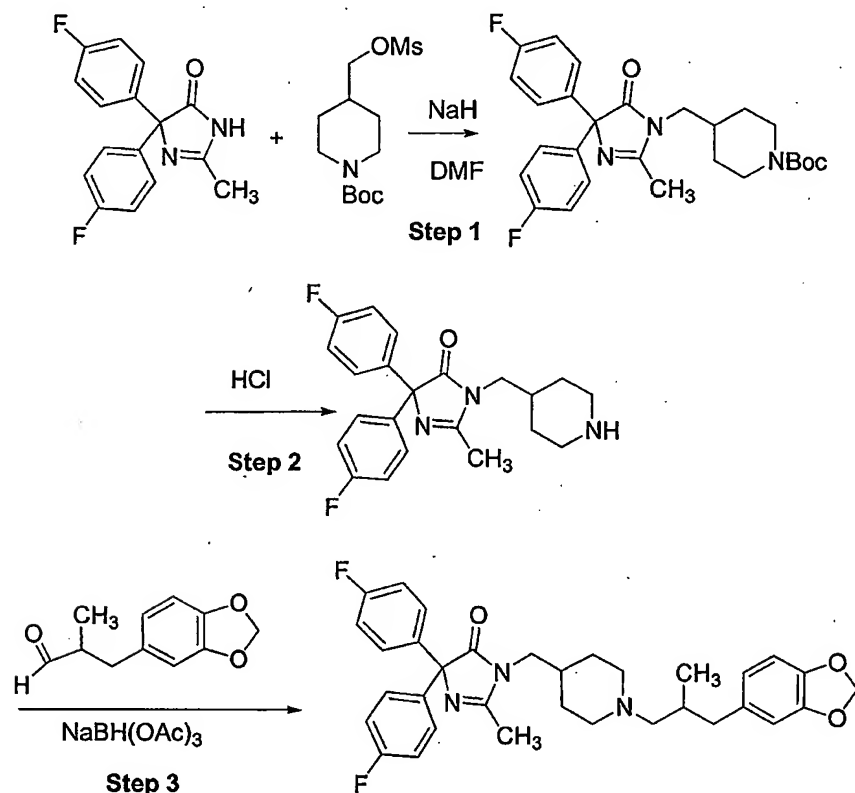
To a solution of 2-methyl-5,5-diphenyl-3-(4-piperidinyl)-3,5-dihydro-4H-imidazol-4-one (0.02 g, 0.06 mmol, 1.0 equiv) in acetonitrile (1 mL) were added (2-bromoethyl)benzene (0.013 g, 0.072 mmol, 1.2 equiv) and potassium carbonate (0.012 g, 0.09 mmol, 1.5 equiv) under an argon atmosphere at rt. The reaction mixture was heated to 80°C under argon for 17 h. The mixture was then quenched with distilled water (2 mL) and extracted with ethyl acetate (3 x 2 mL). The combined extracts were washed with brine (3 mL), dried over sodium sulfate, filtered, and

concentrated under reduced pressure to afford a yellow oil. Purification by HPLC (0-70 acetonitrile/distilled water) yielded the desired product as colorless oil (0.011 g, 40%). LC-MS 438.3 (M+H), RT 2.36 minutes.

[128]

EXAMPLE 14

Preparation of 3-({1-[3-(1,3-benzodioxol-5-yl)-2-methylpropyl]-4-piperidinyl}methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one



[129] Step 1. Preparation of *tert*-butyl 4-{{[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]methyl}-1-piperidinecarboxylate

To the imidazalone (2 g, 6.99 mmol) in dry DMF was added NaH (0.25 g, 10.48 mmol), and the mixture was stirred at rt for 15 minutes under argon. Then, the mesylate (2.05 g, 6.99 mmol) in DMF, was added and the resulting mixture was stirred at 55°C under argon overnight. The mixture was acidified to pH ~5, and concentrated *in vacuo*. The residue was taken up in DCM, washed with water, extracted with DCM, dried over Na₂SO₄, and concentrated *in vacuo*. Residue was purified (20 % EtOAc / Hex) by flash chromatography. Residue triturated with Et₂O and filtered to provide the desired product (1.53 g, 45%). LC-MS M+H 484.0, RT = 3.42 min. ¹H-NMR (CDCl₃-d) δ 7.47 – 7.36 (m, 4 H), 7.05 – 6.96 (m, 4 H), 4.17 – 3.99 (m, 2 H), 3.45 – 3.39 (d,

$J = 7.6$ Hz, 2 H), 3.04 – 2.85 (m, 2 H), 2.68 – 2.55 (br, t, $J = 12.3$ Hz, 2 H), 2.42 (s, 3 H), 1.89 – 1.73 (m, 1 H), 1.44 (s, 9 H), 1.26 – 1.06 (m, 2 H).

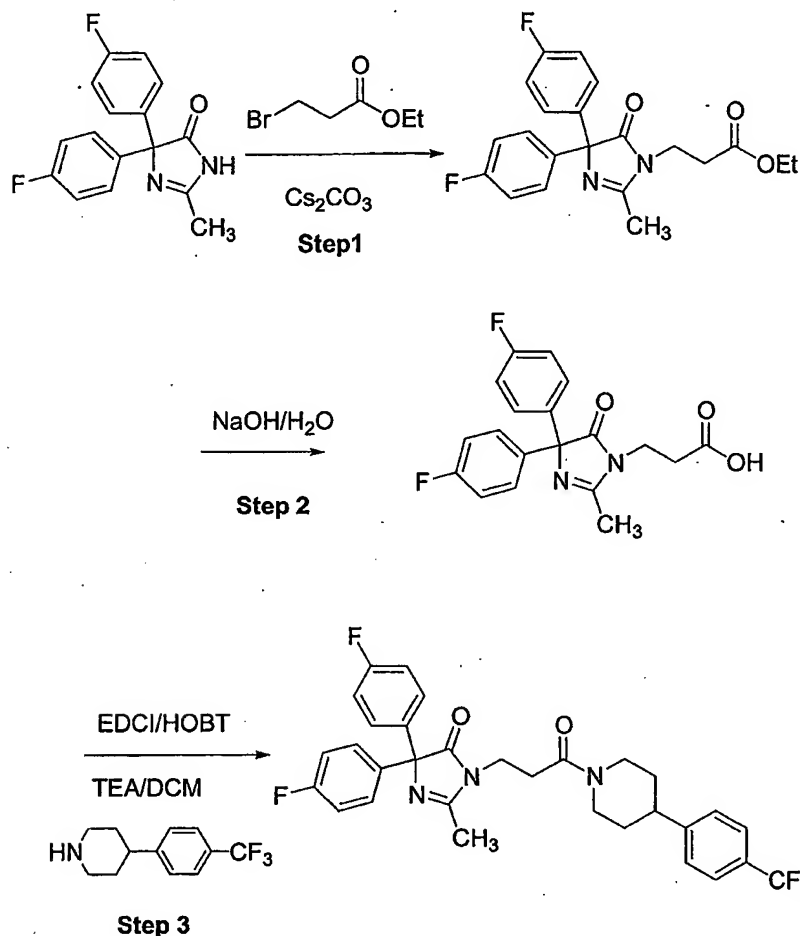
[130] Step 2. Preparation of 5,5-bis(4-fluorophenyl)-2-methyl-3-(4-piperidinylmethyl)-3,5-dihydro-4H-imidazol-4-one

Product (1.53 g, 3.16 mmol) from Step 1 was dissolved in MeOH. HCl (4 M) in dioxane (15.82 mL, 63.28 mmol) was added dropwise and allowed to stir at rt for 1 h. The mixture was concentrated, and residue was dissolved in DCM, washed with NaHCO₃, extracted with DCM, dried over Na₂SO₄, and concentrated *in vacuo* to provide the desired product (1.2 g, 99 %). LC-MS. M+H 384.2, RT = 1.99. The product was used without further purification.

[131] Step 3. Preparation of 3-({1-[3-(1,3-benzodioxol-5-yl)-2-methylpropyl]-4-piperidinyl}methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

To the imidazalone (100 mg, 0.26 mmol) in DCM was added 3-benzo[1,3]dioxol-5-yl-2-methylpropionaldehyde (75.19 mg, 0.39 mmol) and acetic acid (0.27 mL, 4.69 mmol). After stirring for 10 minutes, NaBH(OAc)₃ (165.82 mg, 0.78 mmol) was added, and the resulting solution was stirred at rt overnight. The reaction mixture was washed with water, extracted with DCM, dried over Na₂SO₄, and concentrated *in vacuo*. The residue was taken up on MeOH / CH₃CN and purified by prep HPLC. After the correct fractions were concentrated, they were dissolved in DCM, washed with NaHCO₃, dried over Na₂SO₄, and evaporated *in vacuo* to provide the desired product (99 mg, 68%). LC-MS M+H 560.4, RT 3.01 min. ¹H-NMR (CD₃OD) δ 7.41 – 7.36 (m, 4 H), 7.11 – 7.01 (m, 4 H), 6.75 – 6.60 (m, 3 H), 5.90 – 5.87 (d, $J = 7.2$ Hz, 2 H), 3.56 – 3.54 (d, $J = 7.2$ Hz, 3 H), 3.40 – 3.34 (m, 1 H), 2.97 – 2.94 (d, 6.9 Hz, 2 H), 2.93 – 2.85 (dd, $J = 3.0$ and 12.9 Hz, 1 H), 2.80 – 2.56 (m, 2 H), 2.50 – 2.42 (q, $J = 8.1$ Hz, 1 H), 2.42 – 2.38 (m, 2 H), 2.30 – 2.11 (m, 2 H), 2.07 – 1.94 (m, 1 H), 1.85 – 1.74 (m, 2 H), 1.67 – 1.44 (m, 2 H), 1.01 – 0.97 (d, $J = 6.9$ Hz, 3 H).

[132]

EXAMPLE 15**Preparation 5,5-bis(4-fluorophenyl)-2-methyl-3-(3-oxo-3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one****[133] Step 1. Preparation of ethyl 3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propanoate**

To a solution of 5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one (1.00 g, 3.49 mmol) in anhyd DMF (10 mL) was added benzyltrimethylammonium chloride (0.32 g, 1.75 mmol), cesium carbonate (2.85 g, 8.73 mmol), and ethyl-3-bromopropionate (1.07 g, 5.94 mmol), and the mixture was heated to 120°C for 24 h. The reaction was then quenched with water (30 mL), and extracted with ethyl acetate (2 x 20 mL). The organic layers were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (40% EtOAc / Hex) to afford the desired compound as a yellow oil (0.64 g, 47%). LC-MS M+H 387.3; RT: 2.99 min; R_f : 0.26 (75% EtOAc / Hex).

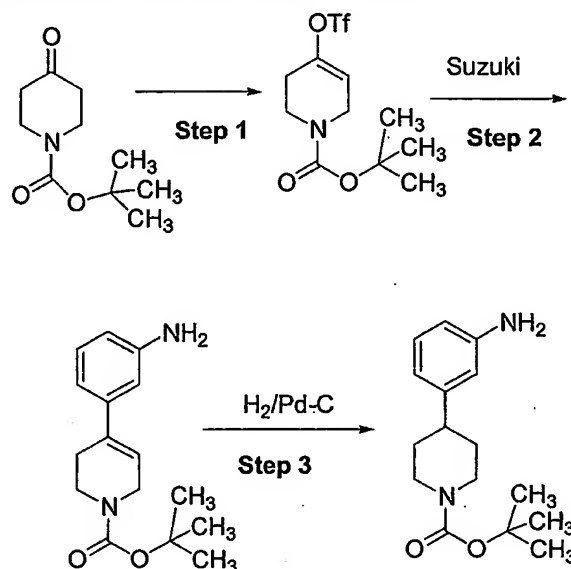
[134] Step 2. Preparation of 3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propanoic acid

To a solution of ethyl 3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propanoate (0.64 g, 1.66 mmol) in ethanol (1 mL) and water (1 mL) was added sodium hydroxide (0.13 g, 3.31 mmol), and the reaction was allowed to stir for 18 h at 80°C. The reaction was quenched with water (30 mL), and extracted with dichloromethane (30 mL). The aqueous layer was then acidified to pH 2 and extracted with dichloromethane (30 mL). The organic layers were combined and dried over MgSO₄, filtered, and concentrated *in vacuo* to afford a white crystalline solid (0.46 g, 78%): LC-MS M + H 359.3, RT: 2.52 min; ¹H-NMR (DMSO-d₆) δ 2.3 (s, 3H), 2.5 (t, *J* = 7.5 Hz, 2H), 3.6 (t, *J* = 7.5 Hz, 2H), 7.1 (m, 4H), 7.3 (m, 4H); R_f: 0.10 (50% EtOAc / Hex).

[135] Step 3. Preparation of 5,5-bis(4-fluorophenyl)-2-methyl-3-(3-oxo-3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one

To a sealed tube was added 3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propanoic acid (0.10 g, 0.28 mmol), HOBT (0.075 g, 0.56 mmol), EDCI (0.10 g, 0.56 mmol), triethylamine (0.12 mL, 0.84 mmol), and 4-(4-trifluoromethylphenyl)-piperidine (0.22 g, 0.84 mmol) in dichloromethane (3 mL). The reaction was then heated to 35°C for 18 h. The reaction was quenched with water (30 mL) and extracted with dichloromethane (30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated *in vacuo* to afford a white crystalline solid. The crude material was then purified by HPLC to give the desired compound as a white solid (0.025 g, 16%): LC-MS M + H 370.4, RT 3.56 min. ¹H-NMR (DMSO-d₆) δ 1.5 (q, *J* = 6 Hz, 2H), 1.9 (t, *J* = 7 Hz, 2H), 2.5 (m, 4H), 2.8 (m, 3H), 3.0 (m, 1 H), 3.9 (m, 3H), 4.7 (m, 1H), 7.0 (m, 4H), 7.2 (m, 2H), 7.4 (m, 4H), 7.6 (2H). R_f: 0.10 (50% EtOAc / Hex).

[136]

EXAMPLE 16**Preparation of *tert*-butyl 4-(3-aminophenyl)-1-piperidinecarboxylate****[137] Step 1. Preparation of *tert*-butyl 4-[[[(trifluoromethyl)sulfonyl]oxy]-3,6-dihydro-1(2H)-pyridinecarboxylate**

n-Butyl lithium (17.33 mL, 27.73 mmol, 1.6 M in hexanes) was added to a solution of diisopropyl amine (3.89 mL, 27.73 mmol) in 6.5 mL of dry THF at -60°C and stirred for 20 minutes while warming to -30°C . The solution was cooled to -60°C , and a white precipitate formed (LDA). THF (18 mL) was added and the reaction was cooled to -72°C . A solution of 4-oxo-1-piperidinecarboxylate (5.00 g, 25.09 mmol) in THF (25 mL) was added dropwise to the reaction mixture, and stirred for 30 minutes. TF_2NPh (9.6 g, 27 mmol) was added to the reaction mixture, and stirred while warming to rt overnight. The reaction mixture was concentrated *in vacuo*, re-dissolved in hexanes:EtOAc (9:1), passed through a plug of alumina (Neutral 60-325 mesh), and the plug was washed with hexanes:EtOAc (9:1). The combined extracts were concentrated to yield 9.0 g of the desired product. ^1H NMR (CDCl_3) δ 6.00 (s, 1H), 4.00 (2 H), 3.56 (t, 2 H), 2.49 (m, 2 H), 1.40 (s, 9 H).

[138] Step 2. Preparation of *tert*-butyl 4-(3-aminophenyl)-3,6-dihydro-1(2H)-pyridinecarboxylate

A mixture of 2 M aq Na_2CO_3 solution (42 mL), triflate from Step 1 (50.0 g, 15.1 mmol), 3-aminophenylboronic acid hemisulfate (3.93 g, 2.11 mmol), lithium chloride (1.91 g, 45.0 mmol), and tetrakis-triphenyl phosphine palladium (0.80 g, 0.75 mmol) in dimethoxyethane (50 mL) was purged with argon and heated at 100°C under an inert atmosphere overnight. The organic layer of the cooled reaction mixture was separated, and the aqueous layer was washed with EtOAc (3x). The combined organic extracts were dried and concentrated *in vacuo*. The crude product was

separated by flash chromatography (silica, EtOAc :Hexane 3:7) to give the product as a yellow oil (2.5 g, 60 %). ^1H NMR (CDCl_3) δ 7.25 (s, 1 H), 7.22 (m, 1H), 6.92 (m, 2 H), 6.84 (m, 1H), 6.02 (s, 1H), 4.1 (m, 2H), 3.62 (2 H), 2.49 (s, 2H), 1.49 (s, 9H), 1.26 (t, 2H).

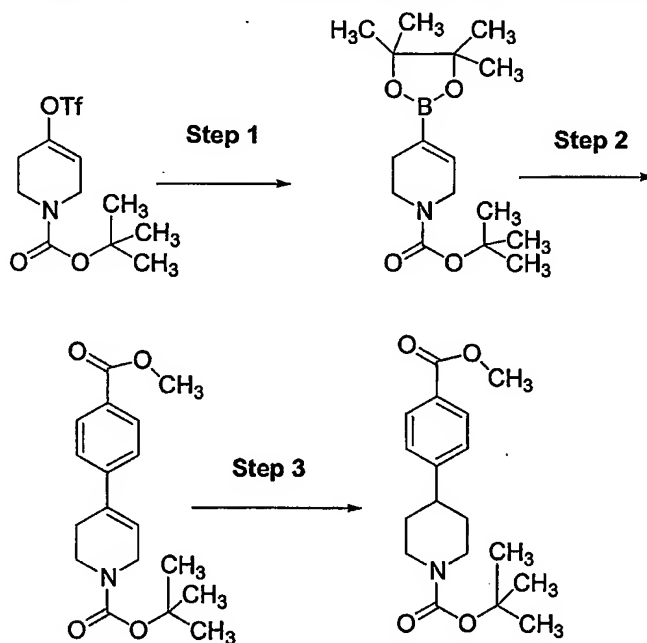
[139] Step 3. Preparation of *tert*-butyl 4-(3-aminophenyl)-1-piperidinecarboxylate

A mixture of *tert*-butyl 4-(3-aminophenyl)-3,6-dihydro-1(2H)-pyridinecarboxylate (3.30 g, 12.03 mmol) and 1.0 g of 10% Pd/C in 200 mL ethanol was hydrogenated at rt for 2 days. The reaction mixture was filtered and washed with ethanol. The combined ethanol extracts were concentrated *in vacuo* to afford the desired product (2.1 g, 63%). LC-MS $M+H$ 276.7, RT 2.05. ^1H NMR (DMSO): δ 6.9 (s, 1H), 6.4 (m, 3H), 4.9 (s, 2H), 4.0 (m, 2H), 2.7 (m, 2H), 1.7 (d, 2H), 1.4 (s, 9H).

[140]

EXAMPLE 17

Preparation of *tert*-butyl 4-[4-(methoxycarbonyl)phenyl]-1 piperidine-carboxylate



[141] Step 1. Preparation of *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-1(2H)-pyridinecarboxylate

To a flask were added bis(pinacolato)diboron (3.37 g, 13.28 mmol), KOAc (3.58 g, 36.46 mmol), PdCl_2dppf (0.27g, 0.36 mmol), dppf (0.2 g, 0.36 mmol), and the contents were flushed with argon. A solution of *tert*-butyl 4-[(trifluoromethyl)sulfonyl]oxy-3,6-dihydro-1(2H)-pyridinecarboxylate from **Example 16** (4.00 g, 12.07 mmol) in dioxane (35 mL) was added, and the mixture was stirred at 80°C overnight. The reaction was allowed to cool to rt, diluted with water (50 mL), and extracted with EtOAc (50 mL). The organic layer was separated, washed with brine (50 mL), and

dried over MgSO_4 and filtered. After evaporation *in vacuo* and purification by flash chromatography (9:1 Hexanes:EtOAc), the product was obtained as a white solid (4.5 g, 100%).

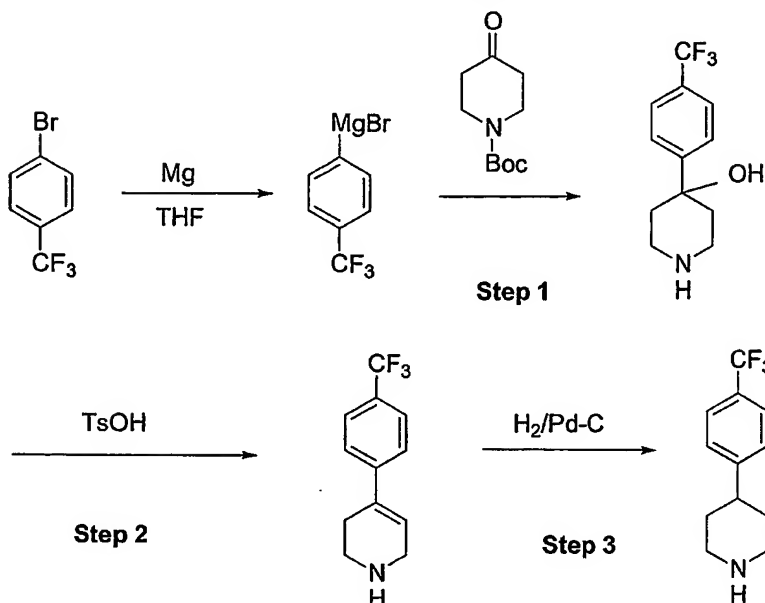
[142] Step 2. Preparation of *tert*-butyl 4-[4-(methoxycarbonyl)phenyl]-3,6-dihydro-1(2H)-pyridinecarboxylate

To an argon flushed flask containing *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-1(2H)-pyridinecarboxylate (1.00 g, 3.23 mmol), K_2CO_3 (1.34 g, 9.70 mmol), and PdCl_2dppf (0.14 g, 0.19 mmol) in DMF (10 mL) was added a solution of methyl 4-bromobenzoate (0.73 g, 3.40 mmol) in DMF (10 mL). The mixture was heated to 80°C and stirred under argon overnight. The mixture was evaporated *in vacuo*, re-dissolved in dichloromethane and adsorbed into silica gel. This solid was purified by flash chromatography (7:3 Hexanes:EtOAc), the desired product was obtained as an clear oil (0.45 g, 43.8%). ^1H NMR (DMSO) 8.01 (d, 2H), 7.7 (d, 2H) 6.16 (s, 1H) 4.11 (m, 2H) 3.91 (s, 3H) 3.66 (t, 2H) 2.56 (br s, 2H) 1.49 (s, 9H).

[143] Step 3. Preparation of *tert*-butyl 4-[4-(methoxycarbonyl)phenyl]-1-piperidine-carboxylate

$\text{Pd}(\text{OH})_2$ (0.02 g, 0.14 mmol) was added into a flask, flushed with argon, and wet with ethanol (4 mL). A solution of ammonium formate (0.09 g, 1.42 mmol) and *tert*-butyl 4-[4-(methoxycarbonyl)phenyl]-3,6-dihydro-1(2H)-pyridinecarboxylate (0.45 g, 1.42 mmol) in ethanol (7 mL) was added, and the reaction was stirred while heating in increments of 5 degrees up to a temperature of 40°C . The catalyst was filtered through Celite[®], and the reaction was evaporated to dryness. LC-MS M+H 319.5, RT 3.34 min. ^1H NMR (CDCl_3) 7.98 (m, 2H), 7.26 (m, 2H), 5.3 (m, 1H), 4.23 (d br, 2H) 3.4 (m, 3H) 2.75 (m, 3H), 1.79 (m, 2H) 1.6 (m, 2H) 1.6 (m, 2H) 1.48 (s, 9H).

[144]

EXAMPLE 18**Preparation of 4-(4-trifluoromethylphenyl)piperidine****[145] Step 1. Preparation of 4-methyl-4-[4-(trifluoromethyl)phenyl] piperidine hydrate**

Magnesium (1 g, 41 mmol, 1 equiv) in THF (30 mL) was cooled to -20°C . A THF (30 mL) solution of 1-bromo-4-(trifluoromethyl)benzene (8.9 g, 40 mmol, 1 equiv) was added into above mixture very slowly. The resulting mixture was stirred for 3 h at rt under argon. The tetrahydrofuran solution of t-butyl 4-oxo-1-piperidinecarboxylate (8.0 g, 43 mmol, 1 equiv) was added slowly into the Grignard THF solution. The mixture was stirred 12 h at rt under argon. The solution volume was reduced *in vacuo* to a final volume of 40 mL. HCl (4 M) in dioxane (40 mL) was added slowly into the mixture. The solution was stirred for 2 h. The mixture was concentrated *in vacuo*. The resulting residue was dissolved into water (150 mL) and the aq solution was extracted with hexanes (20 mL x 3). The pH of the aq solution was adjusted to pH 9 by 2 M sodium hydroxide. Ethyl acetate (30 mL x 3) was used to extract the desired product from aqueous layer. The organic layer was dried over sodium sulfate and concentrated *in vacuo* to yield desired product (8 g, 80 %).

[146] Step 2. Preparation of 4-(4-trifluoromethylphenyl)-1,2,3,6-tetrahydropyridine

To a toluene (35 mL) solution of 4-methyl-4-[4-(trifluoromethyl)phenyl]piperidine hydrate (from Step 1, 6 g, 25 mmol, 1 equiv) was added p-toluenesulfonic acid (20 g, 125 mmol, 5 equiv). The mixture was refluxed for 12 h. Sodium hydroxide (2 M) was used to adjust the pH to 9. The layers were separated and the aqueous layer was washed with ethyl acetate (20 mL x 4). The

combined organic layers were dried over sodium sulfate and concentrated *in vacuo* to yield the desired product (4.5 g, 90 %)

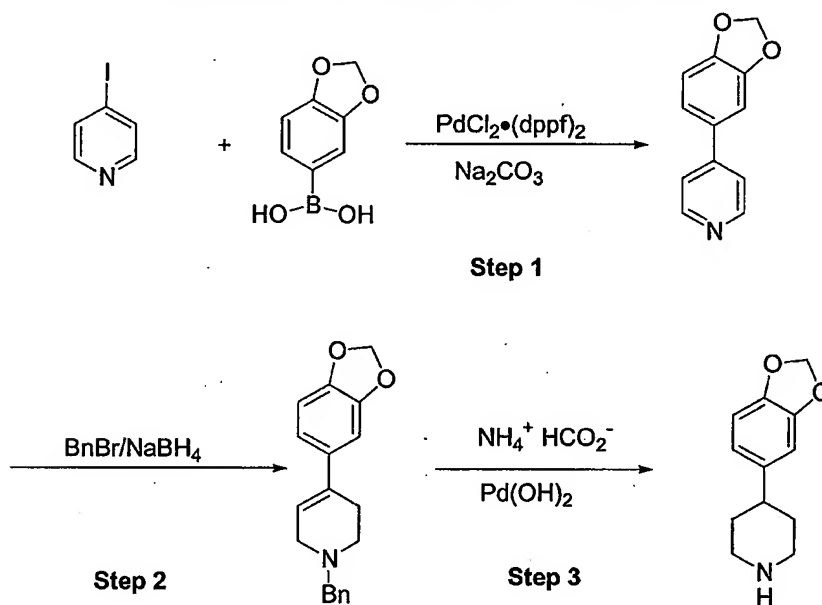
[147] Step 3. Preparation of 4-(4-trifloromethylphenyl)piperidine

4-(4-Trifloromethylphenyl)-1,2,3,6-tetrahydropyridine (4.5 g, 20 mmol) was dissolved into methanol (30 mL) with Pd-C (0.5 g, 10 %) in a Parr shaker bottle. The mixture was shaken under 45 psi for 2 h. The reaction mixture was filtered, the methanol solution was concentrated *in vacuo* to yield desired product (4.5 g, 95%).

[148]

EXAMPLE 19

Preparation of 4-(1,3-benzodioxol-5-yl)piperidine



[149] Step 1. Preparation of 4-(1,3-benzodioxol-5-yl)pyridine

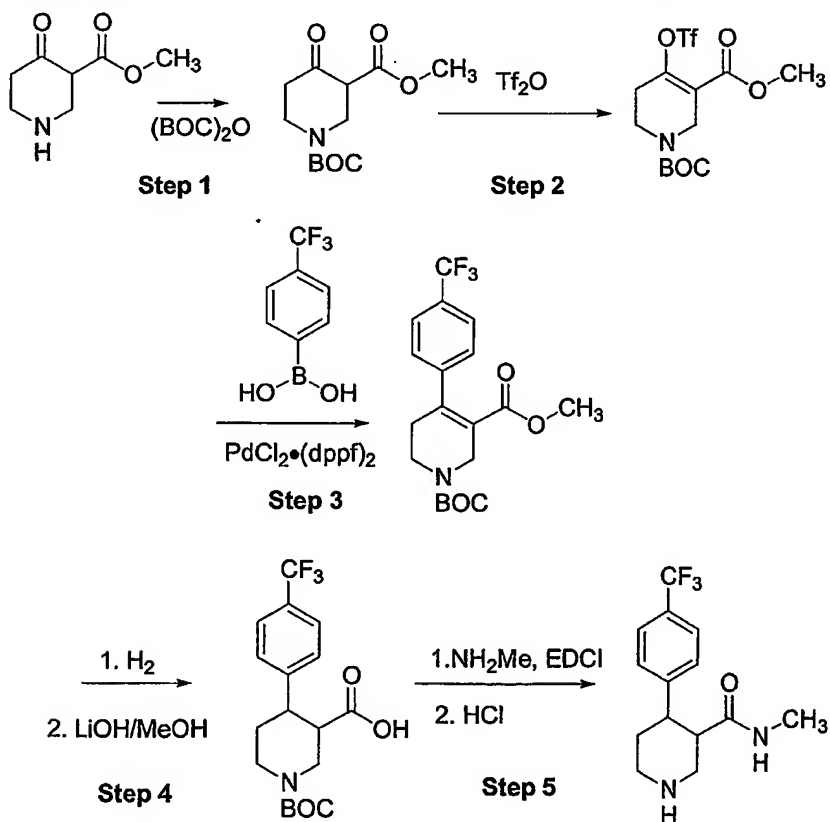
The mixture of 4-iodopyridine (400 mg, 1.9 mmol, 1 equiv), 1,3-benzodioxol-5-yl boronic acid (323 mg, 1.9 mmol, 1 equiv), and $\text{PdCl}_2 (\text{dppf})$ was dissolved in toluene/dioxane (5/1, 20 mL), and then 2 M sodium carbonate aq solution was added to the flask. The mixture was degassed and stirred at 80°C for 12 h. The resulting mixture was filtered to remove solids, and the filtrate was washed by brine (10 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The resulting residue was separated by flash chromatography to yield desired product (350 mg, 90%).

[150] Step 2. Preparation of 4-(1,3-benzodioxol-5-yl)-1-benzyl-1,2,3,6-tetrahydropyridine

4-(1,3-Benzodioxol-5-yl)pyridine (350 mg, 2 mmol, 1 equiv) and benzyl bromide (400 mg, 2.3 mmol, 1.2 equiv) were dissolved in acetone (5 mL). The mixture was stirred for 36 h. The precipitate was collected by filtration. The precipitate was dissolved into methanol (5 mL), and sodium borohydride (100 mg, 2.7 mmol, 1.3 equiv) was added into the flask at 0°C. The mixture was stirred for 1 h at 0°C, and 3 h at rt. Water (5 mL) was slowly added into the flask to quench the reaction. The product was extracted with ethyl acetate (5 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo* to yield the desired product (400 mg, 75 %).

[151] Step 3. Preparation of 4-(1,3-benzodioxol-5-yl)piperidine

To a solution of 4-(1,3-benzodioxol-5-yl)-1-benzyl-1,2,3,6-tetrahydropyridine (350 mg, 1.2 mmol) in methanol (10 mL) was added ammonium formate (600 mg) and palladium hydroxide (35 mg). The mixture was stirred under argon at 80°C for 2 h. The heterogeneous mixture was filtered and the filtrate was concentrated *in vacuo*. The resulting residue was dissolved into methylene chloride (5 mL) and washed with brine (3 X 2 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo* to yield the desired product (200 mg, 80%).

[152]**EXAMPLE 20****Preparation of N-methyl-4-[4-(trifluoromethyl)phenyl]-3-piperidinecarboxamide**

[153] Step 1. Preparation of 1-*tert*-butyl 3-methyl 4-oxo-1,3-piperidinedicarboxylate

To methyl 4-oxo-3-piperidinocarboxylate (3.5 g, 18 mmol) in THF, was added 1 N NaHCO₃ (1.52 mL, 18 mmol), followed by (BOC)₂O (3.94 g, 18 mmol) slowly. The reaction was stirred at rt under argon for 1 h. The reaction was concentrated *in vacuo* and DCM was added, then washed with water, extracted with DCM, dried over Na₂SO₄, and concentrated *in vacuo* to provide the crude product (4.6 g, 99%). ¹H NMR (CD₃OD) δ 4.03 (t, *J* = 1.5 Hz, 2 H), 3.78 (s, 3 H), 3.75 – 3.66 (m, 1 H), 3.56 (t, *J* = 5.9 Hz, 2 H), 2.38 – 2.33 (m, 2 H), 1.47 (s, 9 H).

[154] Step 2. Preparation of 1-*tert*-butyl 3-methyl 4-[[4-(trifluoromethyl)sulfonyl]oxy]-5,6-dihydro-1,3(2H)-pyridinedicarboxylate

The crude product from Step 1 (1 g, 3.89 mmol) in DCM, was cooled to -78°C, DIEA was added (2.03 mL, 11.66 mmol), and then Tf₂O (0.79 mL, 4.66 mmol) was added slowly, and the mixture was stirred at -78°C to rt over 1 h. Water was added to the mixture, and then the mixture was extracted with EtOAc, washed with aq NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo*. Column separation with 10% EtOAc / Hex (1% TEA) to provide the desire product (1.406 g, 93%). ¹H NMR (CD₃OD) δ 4.26 (t, *J* = 2.8 Hz, 2 H), 3.80 (s, 3 H), 3.63 (t, *J* = 5.8 Hz, 2 H), 2.57 – 2.51 (m, 2 H), 1.48 (s, 9 H).

[155] Step 3. Preparation of 1-*tert*-butyl 3-methyl 4-[4-(trifluoromethyl)phenyl]-5,6-dihydro-1,3(2H)-pyridine dicarboxylate

To a solution of 1-*tert*-butyl 3-methyl 4-[[4-(trifluoromethyl)sulfonyl]oxy]-5,6-dihydro-1,3(2H)-pyridinedicarboxylate (5 g, 12.84 mmol) in DME was added 4-trifluoromethylphenylboronic acid (2.68 g, 14.13 mmol) in DME, CsF (3.90 g, 25.68 mmol), and Pd(dppf)₂Cl₂ (1.05 g, 1.28 mmol). The reaction mixture was degassed after each addition. The solution was stirred at reflux (85°C) overnight under argon, filtered through a pad of Celite®, concentrated *in vacuo*, then purified by flash chromatography (5 - 10% EtOAc / Hex) to obtain the pure product as a pale yellow oil (4.65 g, 94%). TLC R_f = 0.4 (50% EtOAc / Hex). ¹H NMR (CD₃OD) δ 7.63 (d, *J* = 7.9 Hz, 2 H), 7.33 (d, *J* = 8.1 Hz, 2 H), 4.25 (t, *J* = 2.6 Hz, 2 H), 3.63 (t, *J* = 5.8 Hz, 2 H), 3.47 (s, 3 H), 2.55 – 2.49 (m, 2 H), 1.50 (s, 9 H).

[156] Step 4. Preparation of 1-(*tert*-butoxycarbonyl)-4-[4-(trifluoromethyl)phenyl]-3-piperidine carboxylic acid

1-*tert*-Butyl 3-methyl 4-[4-(trifluoromethyl)phenyl]-5,6-dihydro-1,3(2H)-pyridine dicarboxylate (2.65 g, 6.88 mmol) was dissolved in a 1:1 mixture of MeOH / EtOAc, and Pd(OH)₂ (4.35 g, 30.94 mmol) and NH₄HCO₃ (4.34 g, 68.76 mmol) were added. The reaction mixture was refluxed for 20 minutes and filtered. The filtrate was concentrated and purified by column chromatography

(20% EtOAc / Hex with 1% TEA) to provide the ester derivative (1.42 g, 53%). TLC R_f = 0.38 (50% EtOAc / Hex).

[157] The above ester (500 mg, 1.29 mmol) was dissolved in THF, cooled to 0°C, then 1 N LiOH (aq) (2.58 mL, 2.58 mmol) was added. MeOH was added until the mixture became homogeneous. The mixture was warmed to rt, and stirred until TLC indicated completion. The pH 5 was adjusted, and the mixture was extracted with DCM, dried over Na₂SO₄, and concentrated *in vacuo* to provide the title compound without further purification (480 mg, 99%). ¹H NMR (CD₃OD): δ 7.58 (d, J = 8.4 Hz, 2 H), 7.44 (d, J = 8.2 Hz, 2 H), 4.40 (d, J = 12.2 Hz, 1 H), 4.24 (dt, J = 2.2, 13.5 Hz, 1 H), 3.06 (td, J = 3.9, 11.7 Hz, 1 H), 2.99 – 2.85 (m, 2 H), 2.75 (td, J = 3.8, 11.3 Hz, 1 H), 1.85 – 1.78 (m, 1 H), 1.72 – 1.58 (m, 1 H), 1.49 (s, 9 H).

[158] Step 5. Preparation of *N*-methyl-4-[4-(trifluoromethyl)phenyl]-3-piperidinecarboxamide

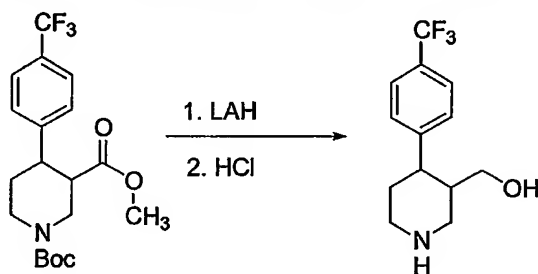
The acid from Step 4 (60 mg, 0.16 mmol) was dissolved in DCM, and amine (0.12 mL, 0.24 mmol), EDCI (60.48 mg, 0.32 mmol), HOBT (42.63 mg, 0.32 mmol), and TEA (0.07 mL, 0.47 mmol) were added. The mixture was stirred at rt overnight, and purified by flash chromatography with 50% EtOAc / Hex to provide amide (61 mg, 98%). R_f 0.38 (50% EtOAc / Hex).

[159] The above amide (61 mg, 0.16 mmol) was dissolved in MeOH, then 4 M HCl in dioxane (0.79 mL, 3.16 mmol) was added dropwise. The solution was stirred at rt overnight. The solution was then concentrated, dissolved residue in DCM, washed with NaHCO₃, dried over Na₂SO₄, and concentrated *in vacuo* to provide the title compound without further purification (45 mg, 99%). LC-MS M+H 287.1, RT 1.35 min.

[160]

EXAMPLE 21

Preparation of {4-[4-(trifluoromethyl)phenyl]-3-piperidinyl}methanol



[161] LiAlH₄ (14.7 mg, 0.39 mmol) was added to anhyd THF in a two-necked flask with a condenser, and the reaction mixture was cooled to -78°C. A solution of the starting ester (100 mg, 0.26 mmol) in THF was added slowly. The reaction mixture was kept at -78°C for 1 h, and then at 0°C for another 1 h. The reaction was quenched at 0°C with 10% KOH (aq) by dropwise addition, and the mixture was stirred at rt for 1 h. The white precipitate was filtered through a Celite® pad,

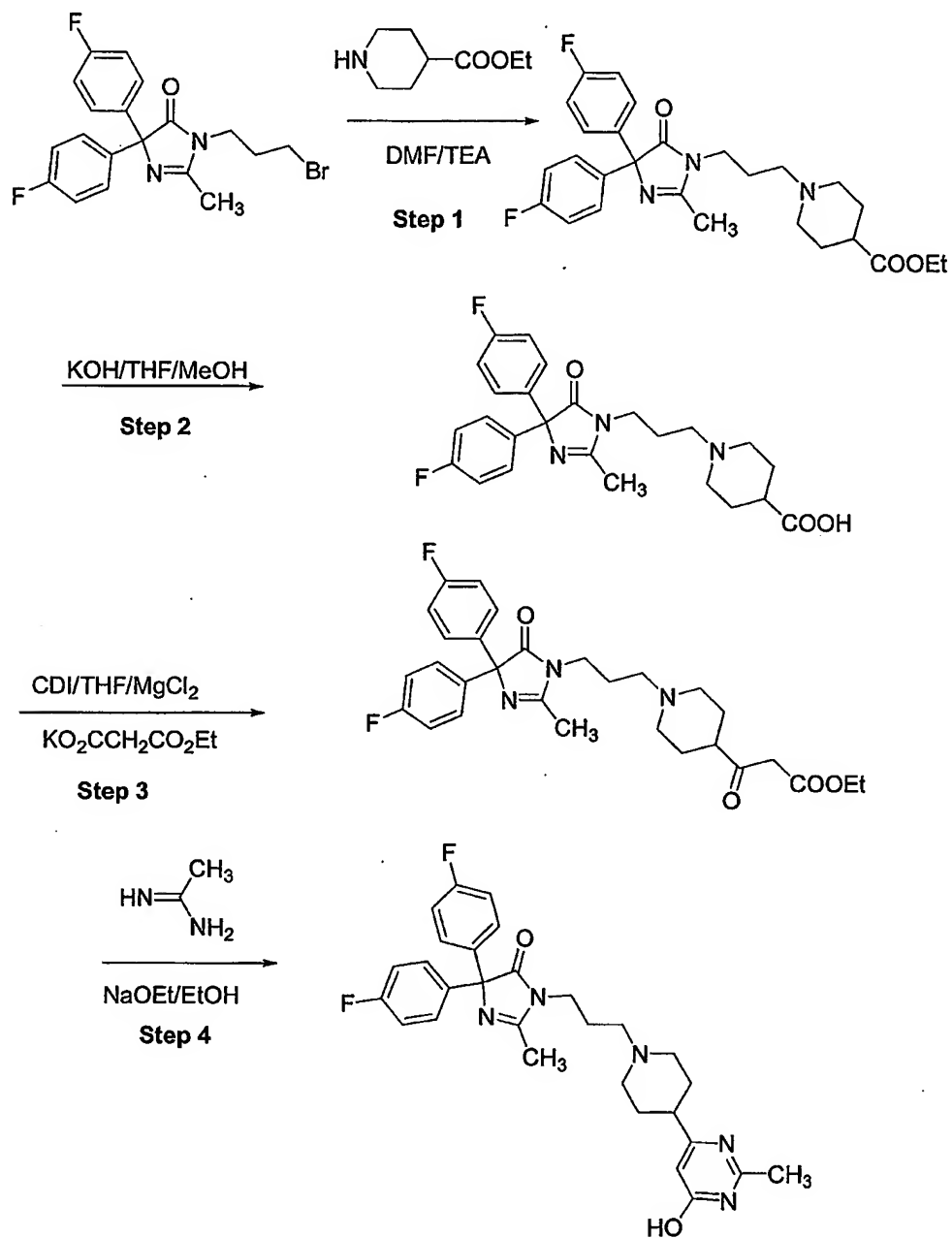
rinsing 3x with diethyl ether. The combined organic filtrates were washed with phosphate buffer (pH ~7), and the aqueous layer was extracted with diethyl ether, dried over Na₂SO₄, and concentrated *in vacuo* to provide the intermediate (92 mg, 99%). LC-MS M+H 359.8, RT 3.89 min. ¹H NMR (CD₃OD) δ 7.67 (d, *J* = 8.5 Hz, 2 H), 7.44 (d, *J* = 8.2 Hz, 2 H), 4.38 (d, *J* = 13.7 Hz, 1 H), 4.28 (d, *J* = 12.0 Hz, 1 H), 3.38 (t, *J* = 11.0 Hz, 1 H), 3.19 (dt, *J* = 4.0, 13.2 Hz, 1 H), 3.04 – 2.93 (m, 2 H), 2.14 – 2.02 (m, 1 H), 1.99 – 1.96 (m, 1 H), 1.73 – 1.64 (m, 1 H), 1.49 (s, 9 H), 1.36 – 1.26 (m, 1 H).

[162] The above intermediate (92 mg, 0.26 mmol) was dissolved in MeOH, then 4 M HCl / dioxane (1.28 mL, 5.12 mmol) was added dropwise. The reaction was stirred at rt overnight. The reaction was then concentrated, dissolved residue in DCM, washed with NaHCO₃, extracted with DCM, dried over Na₂SO₄, and concentrated *in vacuo* to provide the desired product without further purification (66 mg, 99%). LC-MS M+H 260.3, RT 1.04 min. ¹H NMR (CD₃OD) δ 7.62 (d, *J* = 7.8 Hz, 2 H), 7.45 (d, *J* = 8.0 Hz, 2 H), 3.47 (d, *J* = 13.1 Hz, 1 H), 3.32 (d, *J* = 11.4 Hz, 2 H), 3.23 (dd, *J* = 3.7, 11.3 Hz, 2 H), 3.02 (dd, *J* = 2.9, 13.1 Hz, 1 H), 2.87 (td, *J* = 2.6, 12.7 Hz, 1 H), 2.18 – 2.11 (m, 1 H), 2.10 – 2.01 (m, 1 H), 1.77 (d, *J* = 13.6 Hz, 1 H),

[163]

EXAMPLE 22

Preparation of 5,5-bis(4-fluorophenyl)-3-{3-[4-(6-hydroxy-2-methyl-4-pyrimidinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one



[164] Step 1. Preparation of ethyl 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinecarboxylate

To a solution of 3-(3-bromopropyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one (0.5 g, 1.2 mmol, 1.0 equiv) in *N,N*-dimethylformamide (3 mL) were added ethyl 4-piperidine carboxylate (0.3 g, 2 mmol, 2 equiv) and triethylamine (2 mL) under argon atmosphere at rt. The reaction mixture was stirred for 12 h. Ethyl acetate (5 mL) was added to the resulting mixture. The organic layer was washed with brine (3 x 3 mL), and the organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo* to afford a yellow oil. Flash chromatography was used to separate the desired product. The desired product was obtained as colorless oil (0.6 g, 98%). LC-MS M+H 360.3, RT 2.86 min.

[165] Step 2. Preparation of 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinecarboxylic acid

To a solution of ethyl 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinecarboxylate (500 mg, 1 mmol, 1.0 equiv) in THF (6 mL) were added 2M KOH solution (12 mL) and MeOH (3 mL) under an argon atmosphere at rt. The reaction mixture was stirred under argon atmosphere at 60°C for 6 h. Ethyl acetate (20 mL) was added to the resulting mixture. Hydrochloric acid (2 M aq) was added to adjust the pH to 4. The organic layer was washed with brine (5 x 3 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo* to give a white solid (0.48 g, 100%). LC-MS M+H 251.9, RT 3.03 min.

[166] Step 3. Preparation of ethyl 3-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-3-oxopropanoate

To a solution of 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinecarboxylic acid from Step 2 (2.2 g, 5 mmol, 1.0 equiv) in THF (20 mL) was added 1,1'-carbonyldiimidazole (1.0 g, 6 mmol, 1.2 equiv) under argon atmosphere at rt. The reaction mixture was stirred for 30 minutes to make solution A. A mixture of potassium ethyl malonate (1 g, 10 mmol, 2 equiv) and magnesium chloride (0.6 g, 6 mmol, 1.2 equiv) in THF (20 mL) was prepared and stirred at 65°C for 4 h to yield solution B. Then, solution A was added to solution B. The resulting mixture was stirred under argon at rt for 12 h. The mixture was then concentrated *in vacuo* to 20 mL. Water (25 mL) was added to the mixture with vigorous stirring. The resulting white precipitate was filtered as desired product (1.3 g, 60 %). LC-MS M+H 438.3, RT 2.36 min.

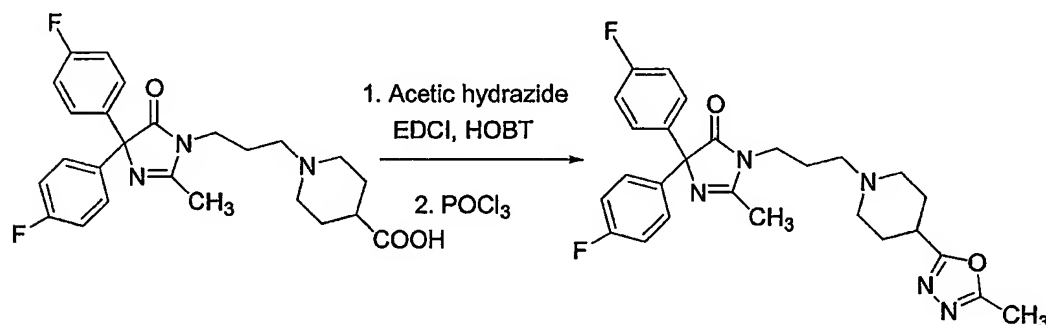
[167] Step 4. Preparation of 5,5-bis(4-fluorophenyl)-3-{3-[4-(6-hydroxy-2-methyl-4-pyrimidinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4*H*-imidazol-4-one

To a solution of acetamidine hydrochloride (50 mg, 0.5 mmol, 2.5 equiv) in ethanol (5 mL) was added sodium ethoxide (50 mg). The mixture was stirred at 80°C for 2 h. Ethyl 3-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]propyl}-4-piperidinyl)-3-oxopropanoate (100 mg, 0.2 mmol, 1 equiv) was added into the mixture. The resulting mixture was refluxed for 12 h under argon atmosphere. Hydrochloric acid (1 M) was used to adjust the pH of solution to 6. The resulting mixture was concentrated *in vacuo*. The resulting residue was dissolved into methanol, and separated by reverse phase HPLC to yield desired product (40 mg, 25 %). LC-MS *M*+*H* 334.1, RT 1.79 min.

[168]

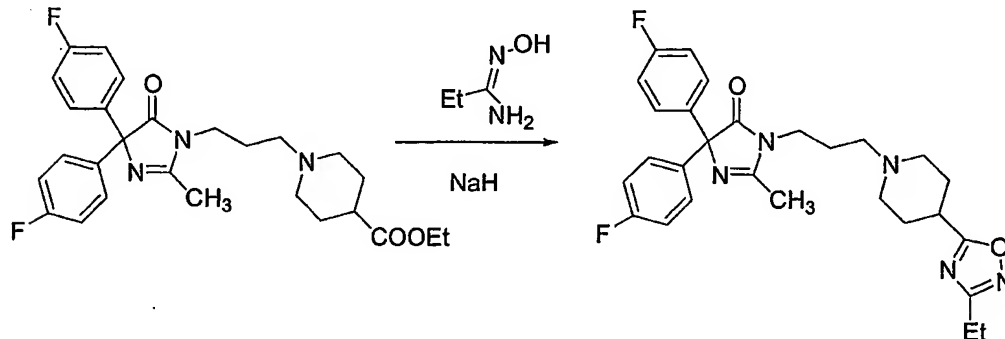
EXAMPLE 23

Preparation of 5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(5-methyl-1,3,4-oxadiazol-2-yl)-1-piperidinyl]propyl}-3,5-dihydro-4*H*-imidazol-4-one



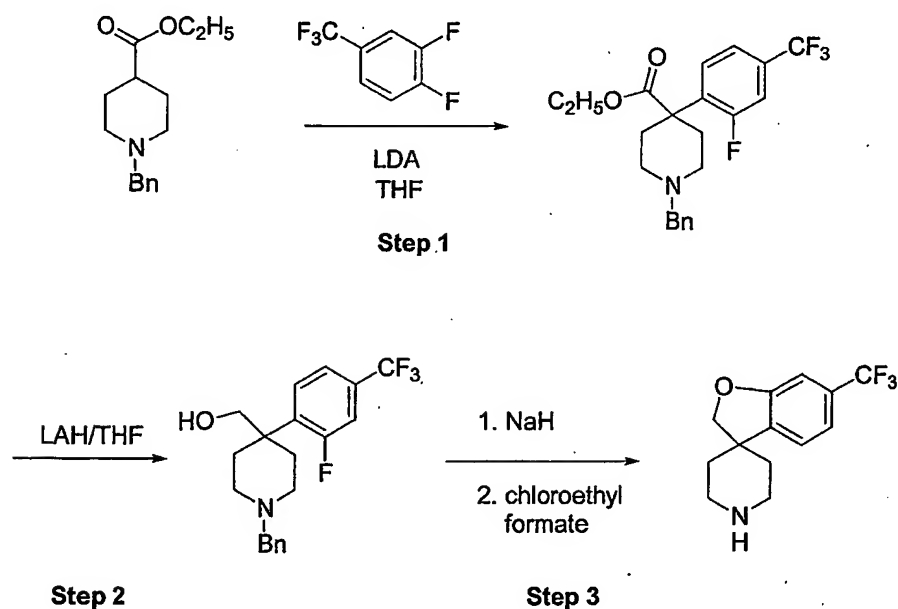
[169] To a solution of 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]propyl}-4-piperidinecarboxylic acid (250 mg, 0.5 mmol, 1.0 equiv) in methylene chloride (10 mL) were added acetic hydrazide (100 mg, 1 mmol, 2 equiv), 1-hydroxbenzotriazole (20 mg, 0.014 mmol), and *N*'-(3-dimethylaminopropyl)-*N*-ethyl carbodiimide hydrochloride (120 mg, 0.6 mmol, 1.2 equiv). The mixture was stirred for 14 h. Methylene chloride (15 mL) was added to the solution followed by 2 M aq sodium bicarbonate. The organic layer was washed with 1 M hydrochloric acid (2 x 3 mL), and brine (2 x 3 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo* to yield the intermediate (130 mg). The crude intermediate was dissolved into acetonitrile (2 mL), and then POCl₃ (1 mL) was added. The mixture was refluxed for 6 h. The mixture was quenched slowly with sodium bicarbonate aq solution to pH 8. Ethyl acetate (5 mL x 3) was used to extract the product. The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The resulting residue was purified by HPLC to yield the desired product (40 mg, 9%).

[170]

EXAMPLE 24**Preparation of 3-{3-[4-(3-ethyl-1,2,4-oxadiazol-5-yl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one**

[171] Ethylamideoxime (50 mg, 0.56 mmol, 1 equiv) was dissolved into THF (20 mL). Sodium hydride (24 mg, 1 mmol) was added to the solution. The mixture was refluxed for 1 h. A THF solution of ethyl 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinecarboxylate (Step 1, **Example 22**, 200 mg, 0.41 mmol, 0.8 equiv) was added to the solution and refluxed for 12 h. Ethyl acetate (3 mL) was added and the organic solution was washed with brine (3 x 3 mL). The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The resulting mixture was purified by preparative TLC to yield the desired product (60 mg, 30 %).

[172]

EXAMPLE 25**Preparation of 6-(trifluoromethyl)spiro[2,3-dihydrobenzo[b]furan-3,4'-piperidine], chloride**

[173] Step 1. Preparation of ethyl 1-benzyl-4-[2-fluoro-4-(trifluoromethyl)phenyl]-4-piperidinecarboxylate

To a solution of *N*-benzylpiperidine-4-carboxylic acid ethyl ester (6.1 g, 24.7 mmol) in 100 mL THF at -78°C was added LDA (14.2 mL of 2M in THF, 28.4 mmol) over 15 minutes. The solution was stirred at -78°C for another 15 minutes, followed by addition of a solution of 3,4-difluorobenzotrifluoride (4.5 g, 24.7 mmol) in 20 mL THF over 15 minutes. The solution was stirred at -78°C for 30 minutes, and then the flask was immersed in an ice-water bath and slowly warmed to rt overnight, followed by treatment of saturated NH_4Cl at 0°C . The mixture was extracted by ethyl acetate (3x). The extracts were combined, washed with water and brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (77% hexane / 18% EtOAc / 5% MeOH) to afford pure desired product (3.52g, 35 %). LC-MS M+H 396.

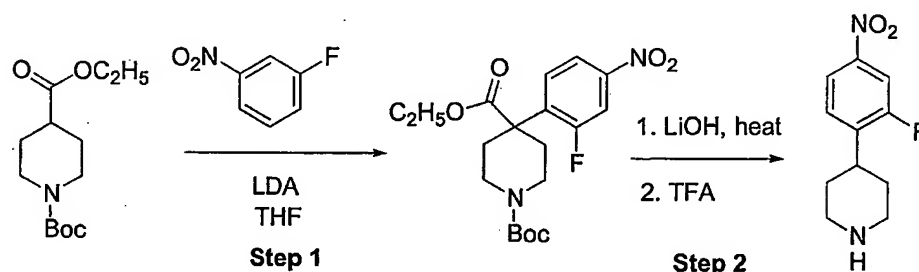
[174] Step 2. Preparation of {1-benzyl-4-[2-fluoro-4-(trifluoromethyl)phenyl]-4-piperidinyl} methanol

LiAlH_4 (464 mg, 12 mmol) was treated with 10 mL THF at 0°C and the mixture was stirred at 0°C for 10 minutes under argon, followed by dropwise addition of the piperidine derivative from Step 1 (2.5 g, 6.1 mmol) in 25 mL THF at 0°C . The mixture was stirred at 0°C for 4 h. The mixture was then treated with cold water (5 mL) followed by 1N NaOH (5 mL) at 0°C . The solid was then removed by filtration. The organic layer was separated, washed with water and brine, dried over MgSO_4 , and evaporated. The residue was purified by column chromatography (50% EtOAc / 45% hexane / 5% MeOH) to afford pure product (2.1 g 94%). LC-MS M+H 368.

[175] Step 3. Preparation of 6-(trifluoromethyl)spiro[2.3-dihydrobenzo[b]furan-3,4'-piperidine], chloride

The piperidine derivative from Step 2 (2.1 g, 5.7 mmol) in 20 mL DMF was treated with NaH (200 mg) at rt under argon and the mixture was heated at 90°C overnight, followed by cooling to rt and treatment with cold water and 100 mL EtOAc:hexane (1:1). The organic layer was separated and the aqueous layer was extracted with 50% EtOAc in hexane. The organic layer and the extracts were combined, washed with water and brine, dried over MgSO_4 , and concentrated to afford pure product, 1.82 g, which was dissolved in 15 mL DCE, followed by treatment of 1-chloroethyl formate (1.65 g, 11.6 mmol) at rt for 30 minutes. The mixture was then heated to reflux for 2 h. Solvent was then removed by evaporation and the residue was treated with methanol under reflux for 2 h. Methanol was then removed and the residue was triturated with hexane to give a solid, which was collected by filtration and washed with ethyl ether to afford pure desired product (1.35 g). LC-MS M+H 257.

[176]

EXAMPLE 26**Preparation of 4-(2-fluoro-4-nitrophenyl)piperidine**

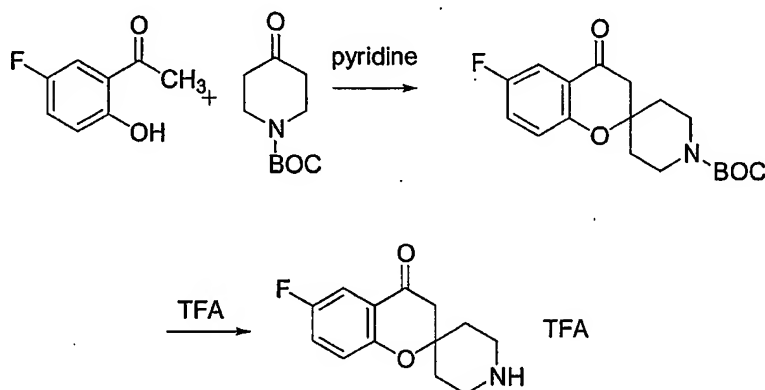
[177] Step 1. Preparation of 1-tert-butyl 4-ethyl 4-(2-fluoro-4-nitrophenyl)-1,4-piperidinedicarboxylate

To a solution of *N*-Boc-piperidine-4-carboxylic acid ethyl ester (2.0 g, 8.3 mmol) in 100 mL THF at -78°C was added LDA (5.0 mL of 2M in THF, 10 mmol) over 15 minutes. The solution was stirred at -78°C for another 15 minutes, followed by addition of a solution of 1-fluoro-3-nitrobenzene (1.2 g, 8.2 mmol) in 20 mL THF over 15 minutes. The solution was stirred at -78°C for 30 minutes, and then the flask was immersed in an ice-water bath and slowly warmed to rt overnight, followed by treatment of saturated NH_4Cl at 0°C . The mixture was extracted by ethyl acetate (3x). The extracts were combined, washed with water and brine, dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by column chromatography (85% hexane / 15% EtOAc) to yield the desired product (1.5 g, 48%). LC-MS $\text{M}+\text{H}$ 383.

[178] Step 2. Preparation of 4-(2-fluoro-4-nitrophenyl)piperidine

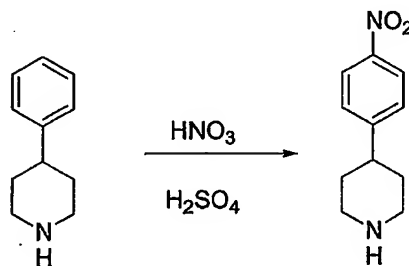
The compound (1.4 g, 3.6 mmol) from Step 1 was dissolved in dioxane (10 mL), followed by treatment of lithium hydroxide (224 mg, 5.4 mmol) in 10 mL water. The mixture was heated to reflux for 5 h, followed by cooling to rt. The mixture was extracted by ethyl ether (3x). The extracts were combined, dried over MgSO_4 , and evaporated to afford pure intermediate, which was treated by 10% TFA in methylene chloride (11 mL) overnight. The solvent was then removed by evaporation and the solid was collected by filtration and washed with ethyl ether to give pure desired product (740 mg). LC-MS $\text{M}+\text{H}$ 245.

[179]

EXAMPLE 27**Preparation of 6-fluorospiro[chromane-2,4'-piperidine]-4-one, 2,2,2-trifluoroacetic acid**

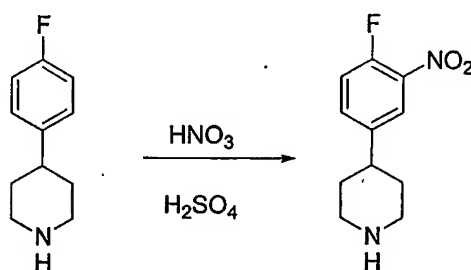
[180] A mixture of 5-fluoro-2-hydroxyacetophenone (4.6 g, 30 mmol), *N*-Boc-4-oxopiperidine (6 g, 30 mmol), and pyridine (4.3 g, 60 mmol) in methanol (150 mL) was heated at reflux overnight, followed by evaporation under reduced pressure to remove solvent. The residue was separated by column (5% MeOH in DCM) to afford 5.5 g intermediate which was treated with 50% TFA in methylene chloride at room temperature overnight. The solvent and excess TFA were removed by evaporation. The residue was triturated by hexane and the solid was collected by filtration and washed by ethyl ether to give pure desired product (5.1 g, 70%). LC-MS $M+H$ 236.

[181]

EXAMPLE 28**Preparation of 4-(4-nitrophenyl)piperidine**

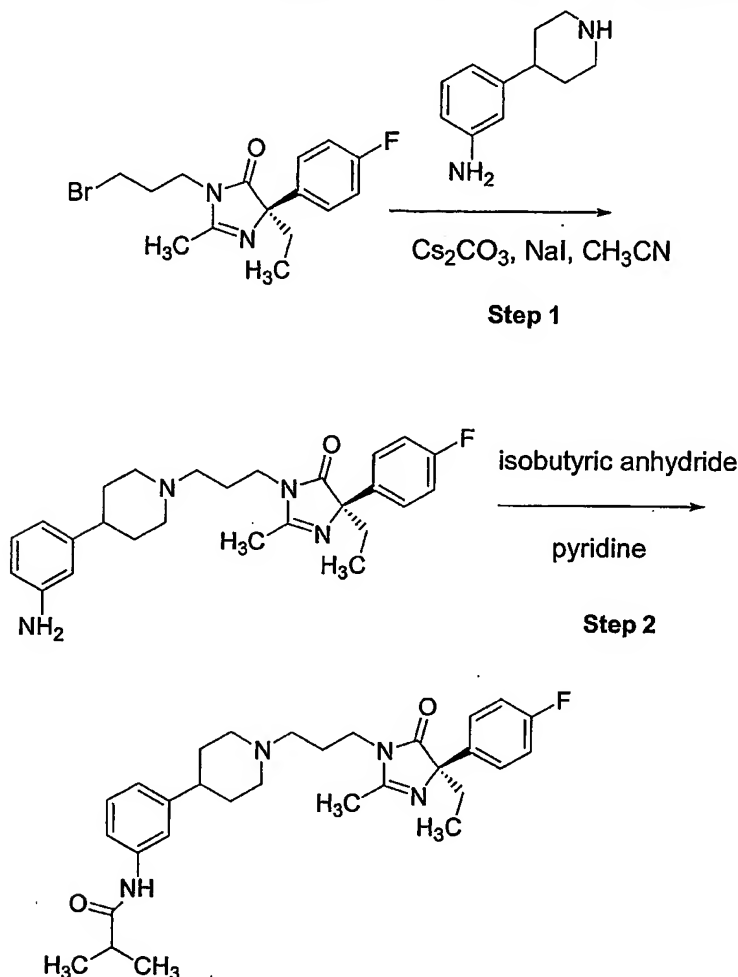
[182] 4-Phenylpiperidine hydrochloride (3 g, 15 mmol) was dissolved in concentrated sulfuric acid (3 g), followed by dropwise addition of concentrated nitric acid at 0°C. The solution was slowly warmed to rt and left at this temperature for 1 day. The mixture was poured into ice water and treated with 1N NaOH until basic. The solution was then extracted by ethyl ether. The extracts were combined, dried over MgSO₄, and evaporated. The residue was recrystallized in ethyl ether to provide pure product (1.5 g). LC-MS $M+H$ 207.

[183]

EXAMPLE 29**Preparation of 4-(4-fluoro-3-nitrophenyl)piperidine**

[184] The title compound was prepared in a similar fashion as **Example 28**, except that the reaction was run at 50°C for 3 days; and the product was isolated directly from the reaction mixture as sulfuric acid salt. LC-MS M+H 225.

[185]

EXAMPLE 30**Preparation of (4R)-N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide****[186] Step 1. Preparation of (5R)-3-{3-[4-(3-aminophenyl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one**

To a solution of (5R)-3-(3-bromopropyl)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one (2.82 g, 8.26 mmol) in acetonitrile (280 mL) were added 4-(3-aminophenyl)piperidine hydrochloride (1.768 g, 8.26 mmol), cesium carbonate (6.73 g, 20.66 mmol), and sodium iodide (0.31 g, 2.07 mmol). The reaction mixture was heated to 60°C with stirring for 24 h, cooled down to rt, and filtered to remove the solid. The solvent acetonitrile was concentrated *in vacuo*. The residue was extracted with ethyl acetate (3 x 50 mL), and washed with water (3 x 50 mL). The organic layer was dried over MgSO_4 , filtered, and concentrated to give the product (2.78 g, 76% yield).

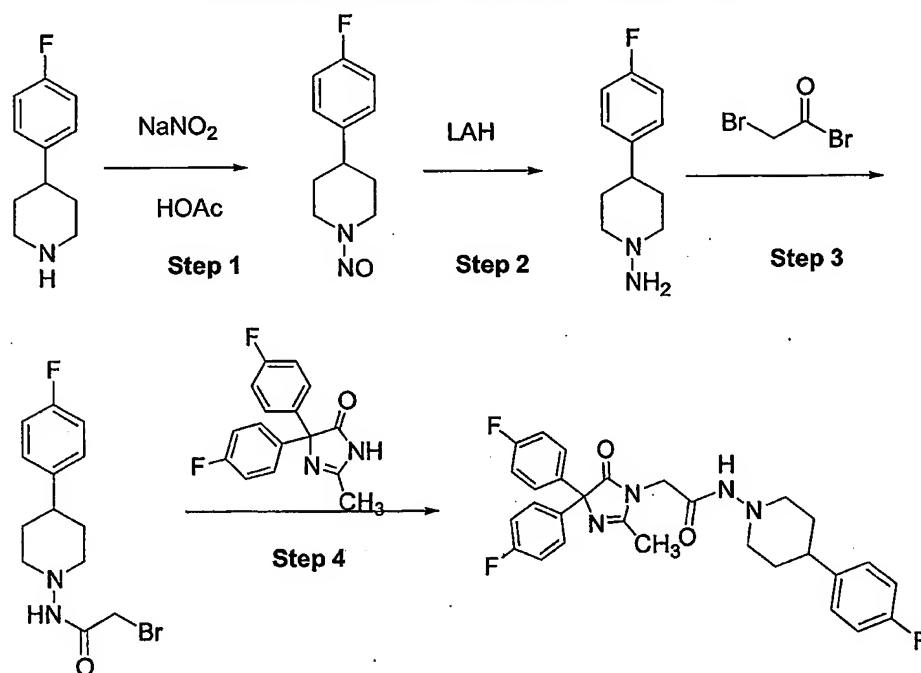
[187] Step 2. Preparation of (4*R*)-*N*-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1*H*-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide

To a solution of (5*R*)-3-{3-[4-(3-aminophenyl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4*H*-imidazol-4-one (2.73 g, 6.25 mmol) in pyridine (50 mL) was slowly added isobutyric anhydride (19.76 g, 124.91 mmol) at 0°C, then reacted at rt for 18 h. It was quenched by adding 30 mL water to the reaction mixture. The solvents were concentrated *in vacuo*, and purified by flash chromatography to give the desired product (1.08 g, 34%). LC-MS: M+H, 507.54, RT 2.37 min. ¹H NMR (CD₃OD) δ 0.81 (t, 3H), 1.21 (d, 6H), 1.75 (t, 2H), 1.82 (m, 4H), 2.05 (m, 4H), 2.38 (m, 2H), 2.44 (m, 2H), 2.50 (m, 1H), 2.61 (m, 1H), 3.00 (t, 2H), 3.35 (s, 1H), 3.61 (t, 2H), 6.97 (d, 1H), 7.07 (t, 2H), 7.11 (t, 1H), 7.39 (t, 2H), 7.57 (m, 2H).

[188]

EXAMPLE 31

Synthesis of 2-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-*N*-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide



[189] Step 1. Synthesis of *N*-nitroso-4-(4-phenyl)piperidine

To a stirred mixture of 4-fluorophenylpiperidine hydrochloride (10 mmol, 2.16 g) and sodium nitrite (20 mmol, 1.38 g) in 40 mL water at 0°C was added dropwise glacial acetic acid. After 30 minutes, the temperature was raised to rt and stirred for 12 hours. The solid was collected by

filtration and washed with water to dried to give pure product (2.0 g, 96%). LC-MS M+H 209, RT 2.64 min.

[190] Step 2. Synthesis of *N*-amino-(4-fluorophenyl)piperidine

A mixture of LiAlH_4 (693 mg, 18.25 mmol) in THF (100 mL) was stirred at rt for 10 minutes, followed by dropwise addition of material from Step 1 (1.9 g, 9.12 mmol) in 30 mL THF. The mixture was then heated to reflux for 2 h under argon, followed by treatment with 1N NaOH at 0°C. The solid was removed by filtration, and the filtrate was dried over MgSO_4 and evaporated to afford pure product (1.45 g, 82%). LC-MS M+H 195, RT 0.95 min.

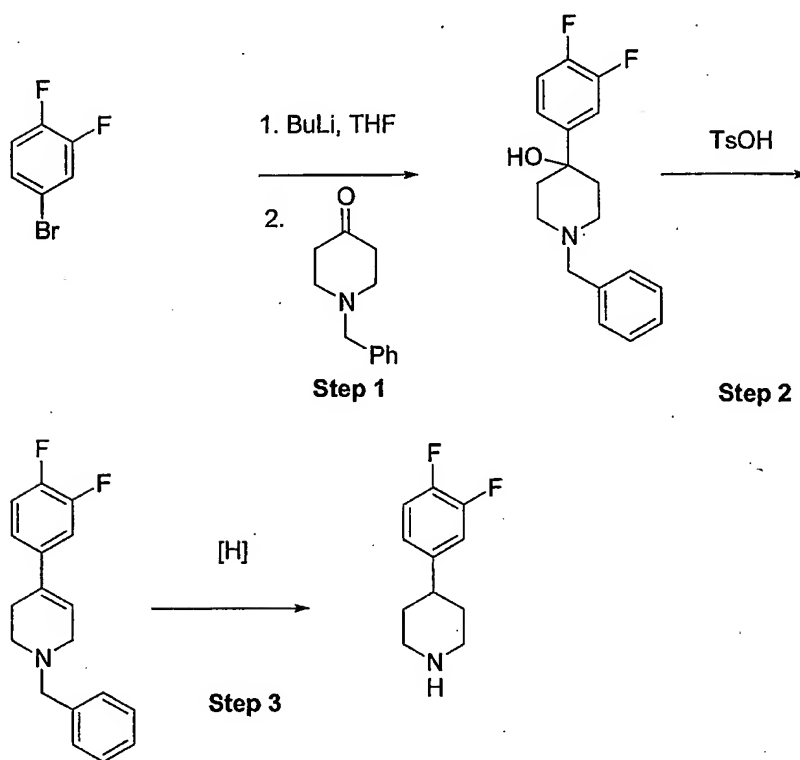
[191] Step 3. Synthesis of *N*-(2-bromoacetamido)-4-(4-phenyl)piperidine

To a solution of *N*-amino-4-(4-fluorophenyl)piperidine (1.43 g, 7.36 mmol) in DMF (5 mL) and dioxane (5 mL) at 0°C was added dropwise 2-bromoacetyl bromide (1.49 g, 7.36 mmol). The solution was stirred at 0°C for 30 minutes at rt overnight. The solution was then diluted with water and extracted with EtOAc (3x). The extracts were combined, dried, and evaporated to give pure product (650 mg, 28%). LC-MS M+H 316, RT 3.29 min.

[192] Step 4. Synthesis of 2-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-*N*-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide

The mixture of product from Step 3 (0.2 mmol, 63 mg), imidazolone (0.2 mmol, 57 mg), cesium carbonate (1 mmol, 328mg), and NaI (0.02 mmol, 3mg) in DMF was stirred at rt for three days. The mixture was then treated with water and extracted with EtOAc. The extracts were combined, dried, and evaporated. The residue was purified by column chromatography (hexane:EtOAc:MeOH 70:25:5) to give pure product (41 mg, 40%). LC-MS M+H 521, RT 3.58 min. ^1H NMR (CD_2Cl_2) δ 7.44 (m, 4H), 7.21 (m, 2H), 7.00 (m, 6H), 4.58 (s, 2H), 3.21 (m, 2H), 2.58 (m, 2H), 2.29 (s, 3H), 1.90 (m, 5H).

[193]

EXAMPLE 32**Synthesis of 4-(3,4-difluorophenyl)piperidine****[194] Step 1. Synthesis of *N*-Benzyl-4-hydroxy-4-(3,4-difluorophenyl)piperidine**

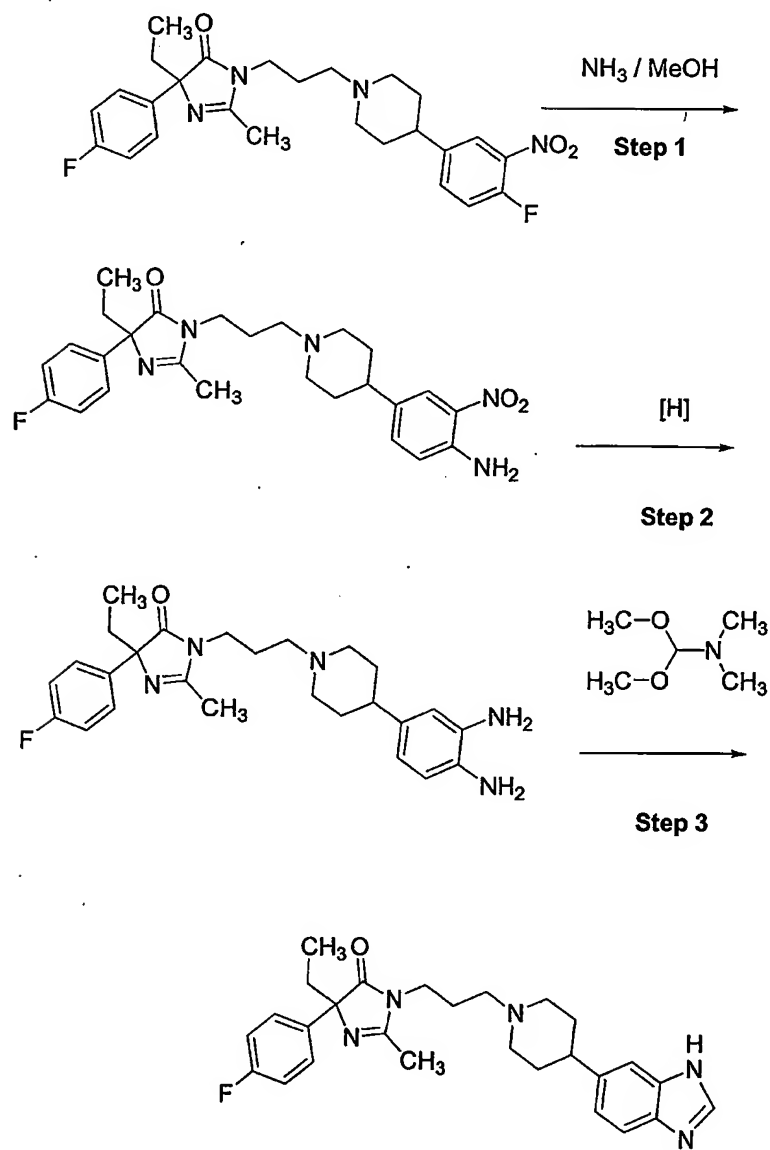
To a solution of *n*-BuLi (33 mmol) in 80 mL THF at -78°C was added dropwise 4-bromo-1,2-difluorobenzene (5.8 g, 30 mmol) in 20 mL THF while stirring. The solution was stirred for 15 minutes after the addition, followed by addition of 1-benzyl-4-oxopiperidine (5.7 g, 30 mmol) in 20 THF. The mixture was slowly warmed to rt overnight, followed by treatment with saturated NH_4Cl , and extraction with EtOAc (3x). The extracts were combined, washed with water and brine, dried, and evaporated to offer a crude product, which was used next step without further purification.

[195] Step 2. Synthesis of *N*-Benzyl-4-(3,4-difluorophenyl)-1,2,5,6-tetrahydropyridine

The mixture of crude product from Step 1 and *p*-toluene sulfonic acid (14 g, 90 mmol) in toluene (150 mL) was refluxed with dean-stark overnight. The solvent was then removed by evaporation and the residue was treated with excess 4N NaOH followed by extraction with EtOAc (3x). The extracts were combined, washed with water and brine, dried and evaporated to provide the crude product.

[196] Step 3. Synthesis of 4-(3,4-difluorophenyl)piperidine hydrochloride

The crude product from Step 2 was dissolved in 2M HCl in MeOH and the mixture was subjected to hydrogenation with 10% Pd-C (1 g) at rt and 55 psi for 3 days. The mixture was then filtered through Celite[®], and the filtrate was evaporated to afford desired product (4.6 g, 66%). LC-MS M+H 198, RT 1.14 min.

[197]**EXAMPLE 33****Synthesis of 3-{3-[4-(1*H*-benzimidazol-6-yl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4*H*-imidazol-4-one**

[198] Step 1. Synthesis of 3-{3-[4-(4-amino-3-nitrophenyl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

The starting materials (490 mg, 1 mmol), prepared in the same way as **Example 29** and **Example 30**, were dissolved in 15 mL 2M ammonia in MeOH in a sealed tube. The mixture was heated at 90°C for 2 days. The solvent was then removed by evaporation to give crude product.

[199] Step 2. Synthesis of 3-{3-[4-(3,4-diaminophenyl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

The crude product from Step 1 was mixed with 10% Pd-C (200 mg) in MeOH and subjected to hydrogenation at rt and 50 psi for 12 h. The mixture was then filtered through Celite®, and the filtrate was evaporated to give crude product (450 mg, 100%). LC-MS M+H 452, RT 0.28 min.

[200] Step 3. Synthesis of 3-{3-[4-(1H-benzimidazol-6-yl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one

To a solution of crude product from Step 2 in DMF was added DMF dimethylacetal. The solution was heated to 80°C overnight. The solvent and excess DMF dimethylacetal were removed by evaporation. The residue was heated to reflux with 6 M HCl for 12 h. Water was then removed again by evaporation and the residue was quenched with NaHCO₃. The mixture was then extracted by EtOAc (3x). The extracts were combined, dried over MgSO₄, and evaporated. The residue was separated by preparative TLC (hexane:EtOAc:MeOH:NH₄OH = 40:40:18:2) to give pure product (27 mg, 13%). LC-MS MH+ 462, RT 0.28 min. ¹HNMR (CD₂Cl₂) δ 8.05 (s, 1H), 7.62 (m, 3H), 7.60 (d, 1H), 7.51 (s, 1H), 7.19 (d, 1H), 7.00 (t, 2H), 3.59 (t, 2H), 3.47 (s, 1H), 3.00 (t, 2H), 2.61 (m, 1H), 2.40 (s, 3H), 2.39 (m, 2H), 2.05 (m, 5H), 1.91 (m, 6H), 0.91 (t, 3H).

Summary of Examples

[201] Using appropriate starting materials and the experimental procedures described above for Examples 1-19, the following compounds in Tables 1 and 2 were prepared. It will be understood by those skilled in the art that some minor modifications to the referenced procedures may have been made, but such modifications do not significantly affect the results of the preparation.

[202] LC-MS characterization of compounds, as listed in the tables, was carried out by using the instrumentation and methods set forth above.

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
1		5,5-bis(4-fluorophenyl)-2-methyl-3-({1-[(5-methyl-3-phenyl-4-isoxazol-5-yl)methyl]-4-piperidinyl)methyl}-3,5-dihydro-4H-imidazol-4-one	Example 14	555.10	2.53	
2		methyl 1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-(4-fluorophenyl)-3-piperidinecarboxylate	Example 2 & 20	564.40	2.55	
3		methyl (3S,4S)-1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-[4-(trifluoromethyl)phenyl]-3-piperidinecarboxylate	Example 2 & 20	614.50	2.71	

Table 1

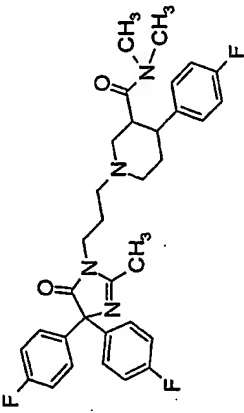
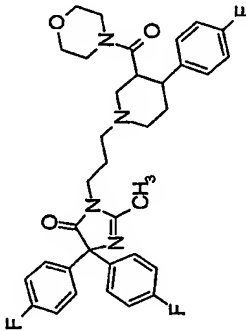
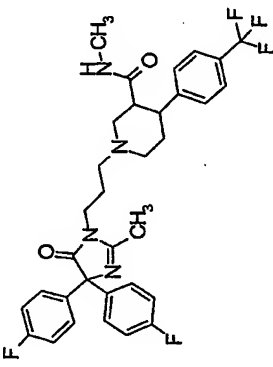
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
4		1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-(4-fluorophenyl)-N,N-dimethyl-3-piperidinecarboxamide	Example 2 & 20	577.40	3.04	
5		5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-3-(4-morpholinylcarbonyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 20	619.20	2.47	
6		1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-N-methyl-4-[4-(trifluoromethyl)phenyl]-3-piperidinecarboxamide	Example 2 & 20	613.20	2.61	

Table 1

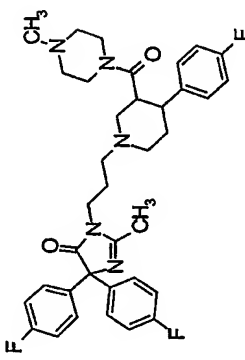
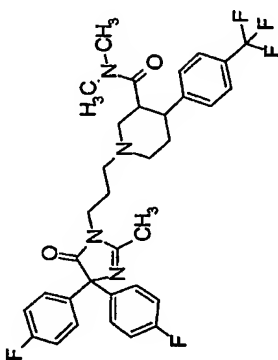
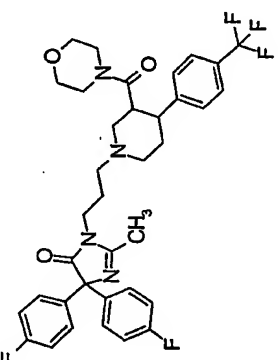
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
7		5,5-bis(4-fluorophenyl)-3-(3-(4-(4-fluorophenyl)-3-[(4-methyl-1-piperazinyl)carbonyl]-1-piperidinyl)propyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 20	632.20	2.11	
8		1-[3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl]-N,N-dimethyl-4-[4-(trifluoromethyl)phenyl]-3-piperidinecarboxamide	Example 2 & 20	627.10	2.77	
9		5,5-bis(4-fluorophenyl)-3-(3-(3-(4-morpholinylcarbonyl)-4-[4-(trifluoromethyl)phenyl]-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 20	669.20	2.62	

Table 1

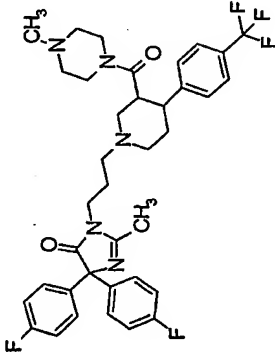
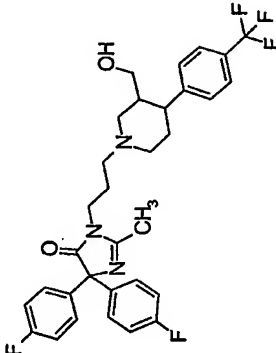
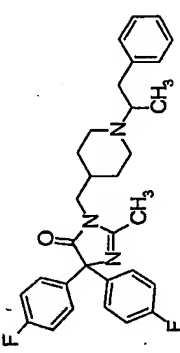
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
10		5,5-bis(4-fluorophenyl)-2-methyl-3-((3-[(4-methyl-1-piperazinyl)carbonyl]-4-[(trifluoromethyl)phenyl]-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 20	682.20	2.24	
11		5,5-bis(4-fluorophenyl)-3-((3-((3-(hydroxymethyl)-4-[(trifluoromethyl)phenyl]-1-piperidinyl)propyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 20	586.50	2.56	
12		5,5-bis(4-fluorophenyl)-2-methyl-3-[(1-(1-methyl-2-phenylethyl)-4-piperidinyl)methyl]-3,5-dihydro-4H-imidazol-4-one	Example 14	502.40	2.44	

Table 1

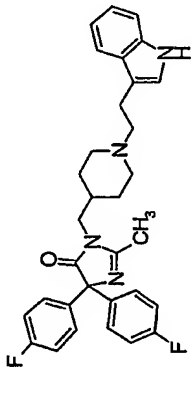
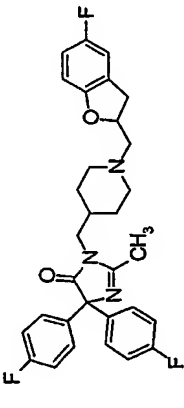
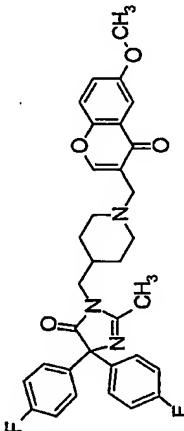
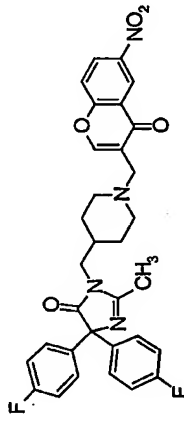
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
13		5,5-bis(4-fluorophenyl)-3-({1-[2-(1H-indol-3-yl)ethyl]-4-piperidinyl)methyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	527.30	2.48	
14		3-({1-[(5-fluoro-2,3-dihydro-1-benzofuran-2-yl)methyl]-4-piperidinyl)methyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	534.50	2.48	
15		5,5-bis(4-fluorophenyl)-3-({1-[6-methoxy-4-oxo-4H-chromen-3-yl)methyl]-4-piperidinyl)methyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	572.10	2.45	
16		5,5-bis(4-fluorophenyl)-3-({1-[6-nitro-4-oxo-4H-chromen-3-yl)methyl]-4-piperidinyl)methyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	587.10	2.46	

Table 1

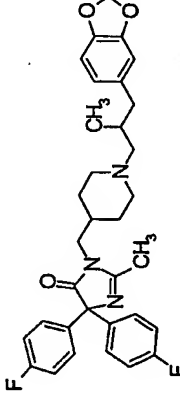
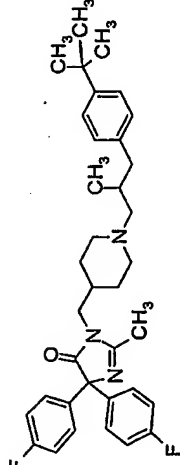
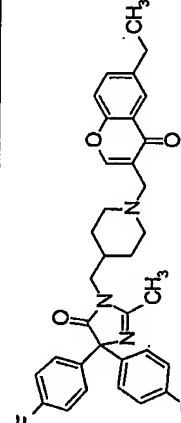
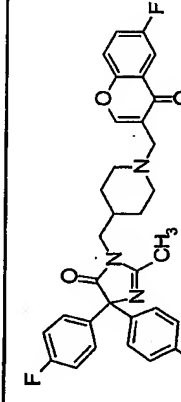
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
17		3-((1-[3-(1,3-benzodioxol-5-yl)-2-methylpropyl]-4-piperidinyl)methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	560.40	3.08	
18		3-((1-[3-(4-tert-butylphenyl)-2-methylpropyl]-4-piperidinyl)methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	572.50	3.39	
19		3-((1-[6-ethyl-4-oxo-4H-chromen-3-yl)methyl]-4-piperidinyl)methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	570.10	2.61	
20		3-((1-[6-fluoro-4-oxo-4H-chromen-3-yl)methyl]-4-piperidinyl)methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	560.70	2.93	

Table 1

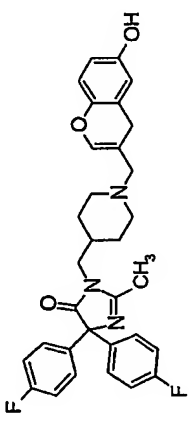
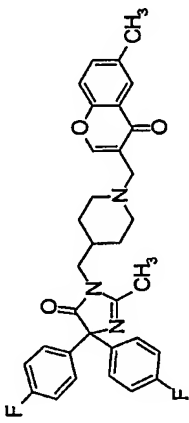
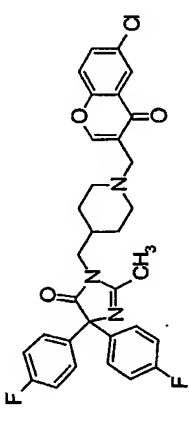
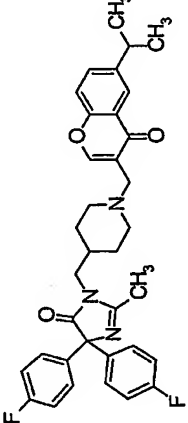
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
21		5,5-bis(4-fluorophenyl)-3-({1-[(6-hydroxy-4H-chromen-3-yl)methyl]-4-piperidyl}methyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	544.20	2.86	
22		5,5-bis(4-fluorophenyl)-2-methyl-3-({1-[(6-methyl-4-oxo-4H-chromen-3-yl)methyl]-4-piperidyl}methyl)-3,5-dihydro-4H-imidazol-4-one	Example 14	556.50	3.00	
23		3-({1-[(6-chloro-4-oxo-4H-chromen-3-yl)methyl]-4-piperidyl}methyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	576.10	2.58	
24		5,5-bis(4-fluorophenyl)-3-({1-[(6-isopropyl-4-oxo-4H-chromen-3-yl)methyl]-4-piperidyl}methyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	584.10	2.72	

Table 1

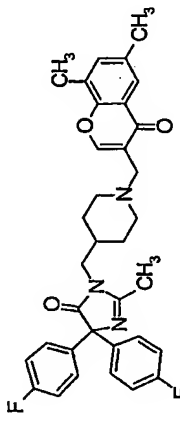
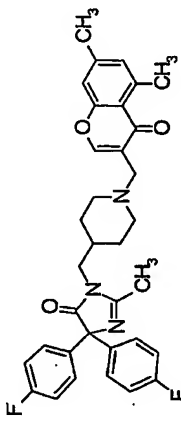
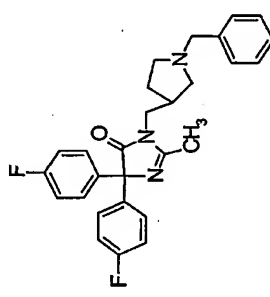
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
25		3-[(1-[(6,8-dimethyl-4-oxo-4H-chromen-3-yl)methyl]-4-piperidinyl)methyl]-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	570.10	2.62	
26		3-[(1-[(5,7-dimethyl-4-oxo-4H-chromen-3-yl)methyl]piperidin-4-yl)methyl]-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	570.10	2.65	
27		3-[(1-benzyl-3-pyrrolidinyl)methyl]-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	460.30	2.32	

Table 1

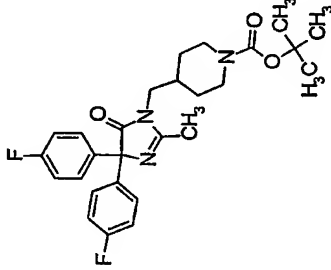
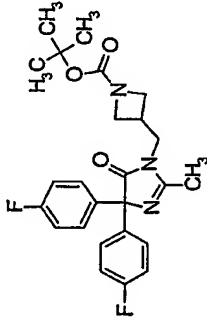
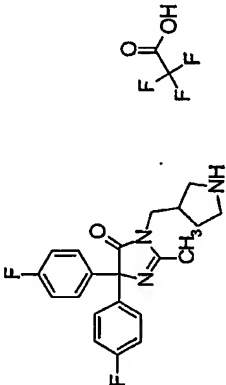
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
28		tert-butyl 4-[[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]methyl]piperidinecarboxylate	Example 14	484.10	3.48	
29		tert-butyl 3-[[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]methyl]azetidinecarboxylate	Example 14	456.10	3.22	
30		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-pyrrolidinylmethyl)-3,5-dihydro-4H-imidazol-4-one	Example 14	370.20	2.01	

Table 1

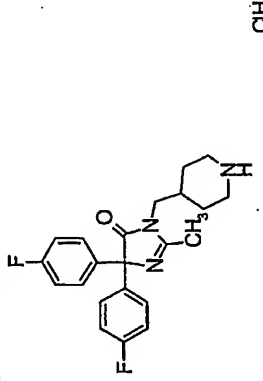
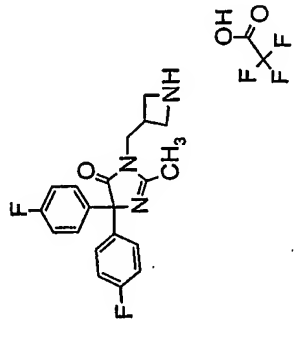
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
31		5,5-bis(4-fluorophenyl)-2-methyl-3-(4-piperidinylmethyl)-3,5-dihydro-4H-imidazol-4-one	Example 14	384.20	1.99	
32		3-(3-azetidinylmethyl)-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 14	356.20	2.63	

Table 1

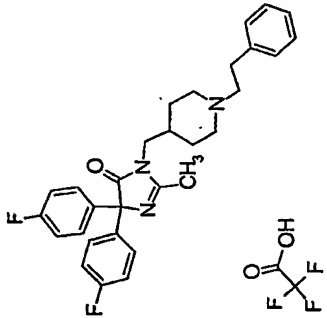
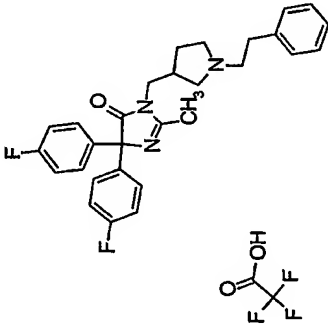
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
33		5,5-bis(4-fluorophenyl)-2-methyl-3-[[1-(2-phenylethyl)-4-piperidinylmethyl]-3,5-dihydro-4H-imidazol-4-one	Example 14	488.40	2.42	
34		5,5-bis(4-fluorophenyl)-2-methyl-3-[[1-(2-phenylethyl)-3-pyrrolidinylmethyl]-3,5-dihydro-4H-imidazol-4-one	Example 14	474.30	3.08	

Table 1

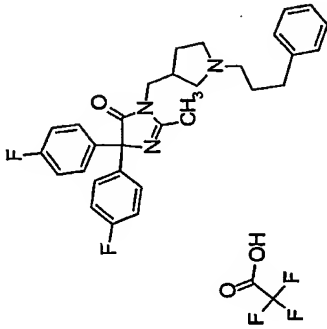
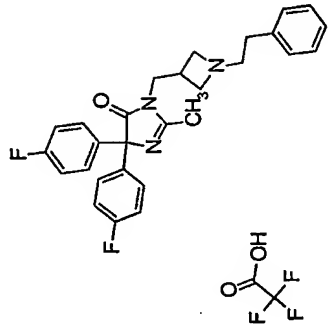
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
35		5,5-bis(4-fluorophenyl)-2-methyl-3-[[1-(3-phenylpropyl)-3-pyrrolidinylmethyl]-3,5-dihydro-4H-imidazol-4-one	Example 14	488.30	2.56	
36		5,5-bis(4-fluorophenyl)-2-methyl-3-[[1-(2-phenylethyl)-3-azetidylmethyl]-3,5-dihydro-4H-imidazol-4-one	Example 14	460.20	2.42	

Table 1

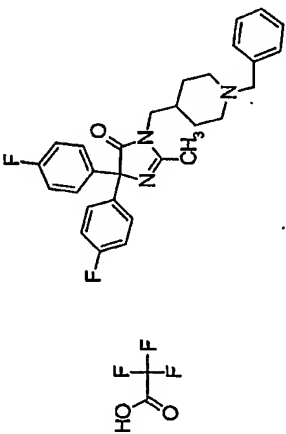
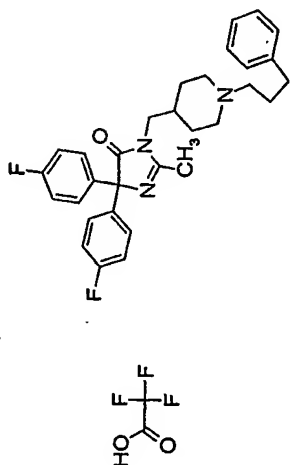
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
37		3-[(1-benzyl-4-piperidinyl)methyl]-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 14	474.40	2.33	
38		5,5-bis(4-fluorophenyl)-2-methyl-3-[(1-(3-phenylpropyl)-4-piperidinyl)methyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 14	502.40	2.50	

Table 1

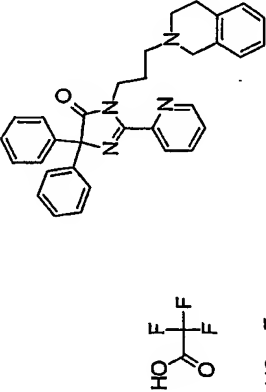
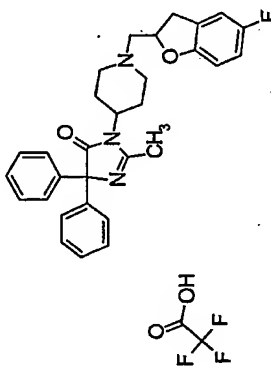
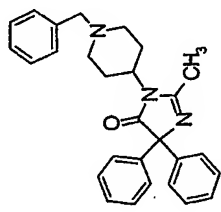
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
39		3-[(3,4-dihydro-2(1H)-isoquinolinyl)propyl]-5,5-diphenyl-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	487.20	2.50	
40		3-{1-[(5-fluoro-2,3-dihydro-1-benzofuran-2-yl)methyl]-4-piperidinyl}-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	484.20	2.45	
41		3-(1-benzyl-4-piperidinyl)-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one	Example 13	424.30	2.24	

Table 1

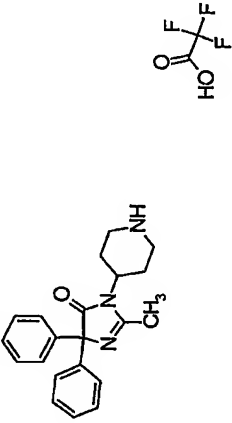
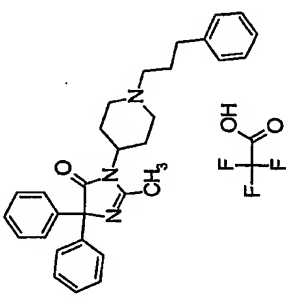
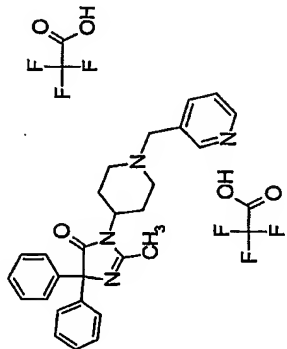
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
42		2-methyl-5,5-diphenyl-3-(4-piperidinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	334.20	1.87	
43		2-methyl-5,5-diphenyl-3-[1-(3-phenylpropyl)-4-piperidinyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	452.30	2.41	
44		2-methyl-5,5-diphenyl-3-[1-(3-pyridinylmethyl)-4-piperidinyl]-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 13	425.10	1.74	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
45		3-{1-[2-(1H-indol-3-yl)ethyl]-4-piperidinyl}-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	477.20	2.41	
46		2-methyl-3-{1-[2-(4-nitrophenyl)ethyl]-4-piperidinyl}-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	483.20	2.37	
47		3-{1-[2-(4-fluorophenyl)ethyl]-4-piperidinyl}-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	456.30	2.38	
48		3-{1-[2-(5-chloro-1-benzothien-3-yl)methyl]-4-piperidinyl}-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	514.10	2.59	

Table 1

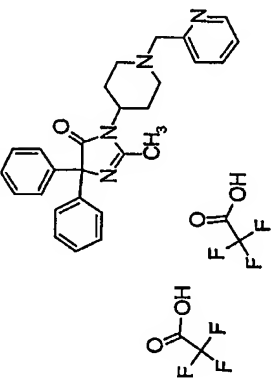
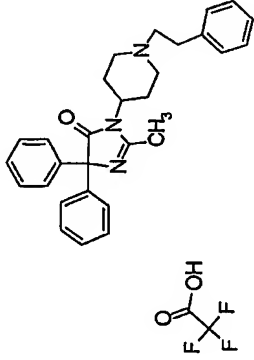
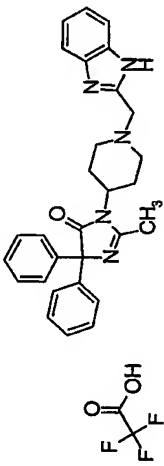
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
49		2-methyl-5,5-diphenyl-3-[1-(2-pyridinylmethyl)-4-piperidinyl]-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 13	425.30	1.96	
50		2-methyl-5,5-diphenyl-3-[1-(2-phenylethyl)-4-piperidinyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	438.30	2.36	
51		3-[1-(1H-benzimidazol-2-ylmethyl)-4-piperidinyl]-2-methyl-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 13	464.20	2.60	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
52		methyl (3S,4S)-1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-phenyl-3-piperidinecarboxylate	Example 2 & 20			
53		ethyl 3-(1-{3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)benzoate	Example 2 & 19	623.10	2.85	
54		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(4-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	505.30	1.80	

Table 1

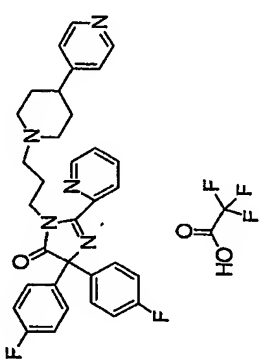
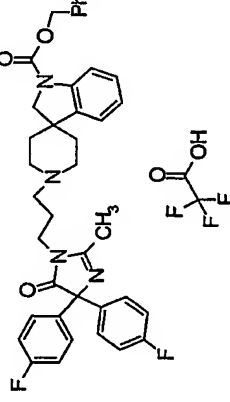
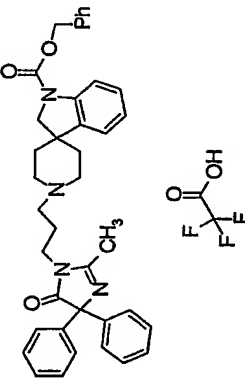
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
55		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-{[4-(4-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	552.30	2.10	
56		phenylmethyl 10-[3-{4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-2-imidazolyl]propyl]spiro[indoline-3,4'-piperidine]carboxylate, 2,2,2-trifluoroacetic acid	Example 2	649.50	2.81	
57		phenylmethyl 10-[3-(2-methyl-5-oxo-4,4-diphenyl-2-imidazolyl)propyl]spiro[indoline-3,4'-piperidine]carboxylate, 2,2,2-trifluoroacetic acid	Example 2	613.50	2.69	

Table 1

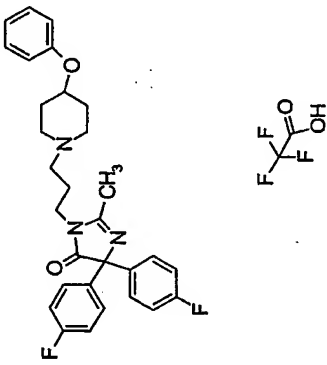
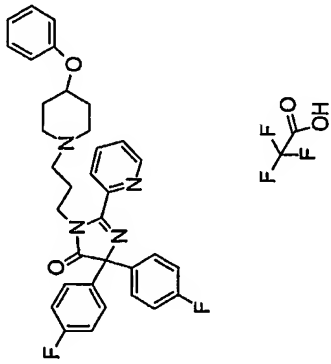
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
58		5,5-bis(4-fluorophenyl)-2-methyl-3-[3-(4-phenoxy-1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one	Example 2	504.30	3.19	
59		5,5-bis(4-fluorophenyl)-3-[3-(4-phenoxy-1-piperidinyl)propyl]-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	567.30	3.44	

Table 1

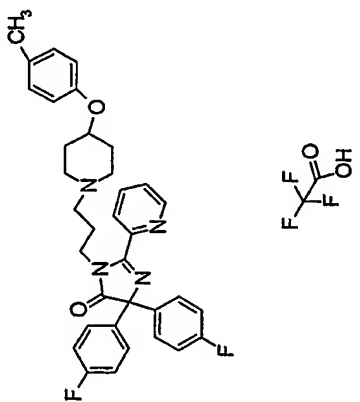
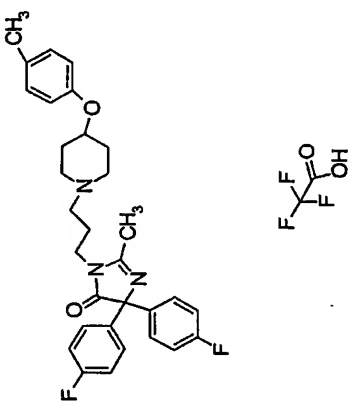
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
60		5,5-bis(4-fluorophenyl)-3-{3-[4-(4-methylphenoxy)-1-piperidinyl]propyl}-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	581.30	3.47	
61		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(4-methylphenoxy)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2	518.30	3.22	

Table 1

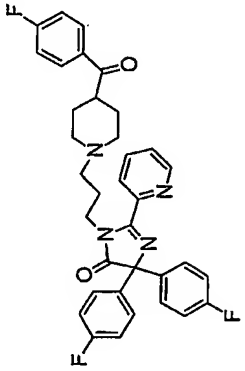
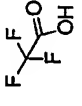
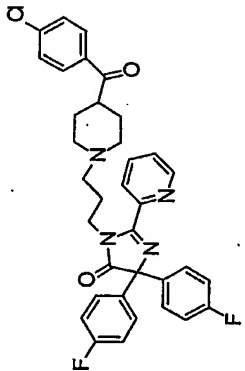
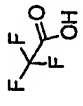
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
62	 	3-{3-[4-(4-fluorobenzoyl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	597.30	3.43	
63	 	3-{3-[4-(4-chlorobenzoyl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	613.30	3.52	

Table 1

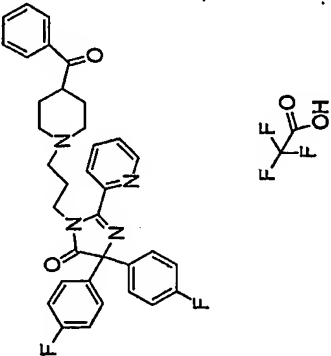
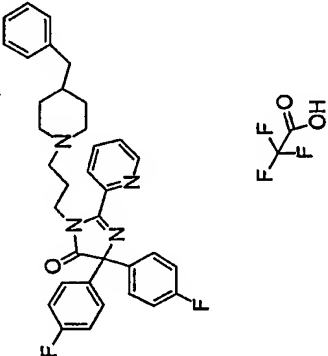
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
64		3-[3-(4-benzoyl-1-piperidinyl)propyl]-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	579.40	3.35	
65		3-[3-(4-benzyl-1-piperidinyl)propyl]-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	565.30	3.38	

Table 1

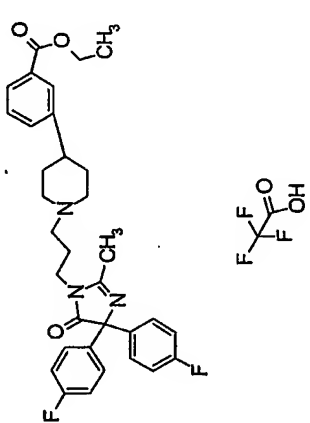
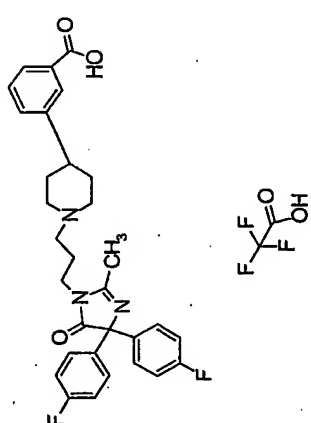
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
66		ethyl 3-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidyl)benzoate	Example 2 & 19	560.20	2.61	
67		3-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidyl)benzoic acid	Example 2 & 19	532.10	2.32	

Table 1

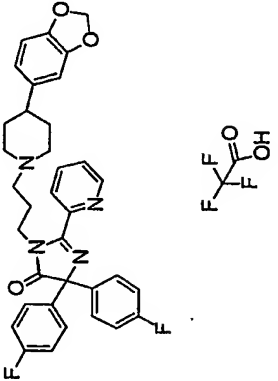
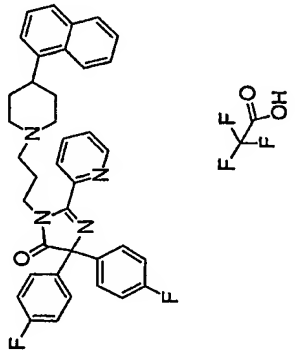
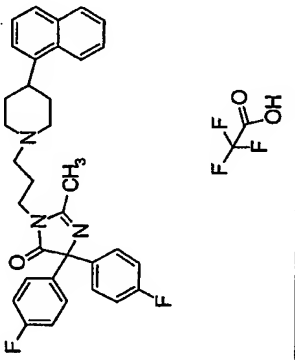
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
68		3-{3-[4-(1,3-benzodioxol-5-yl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	595.10	2.81	
69		5,5-bis(4-fluorophenyl)-3-{3-[4-(1-naphthyl)-1-piperidinyl]propyl}-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	601.10	2.95	
70		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(1-naphthyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	538.20	2.63	

Table 1

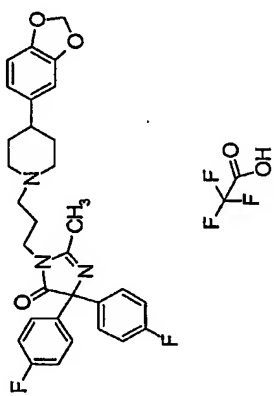
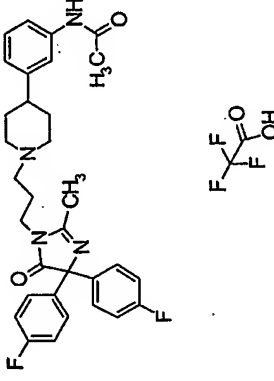
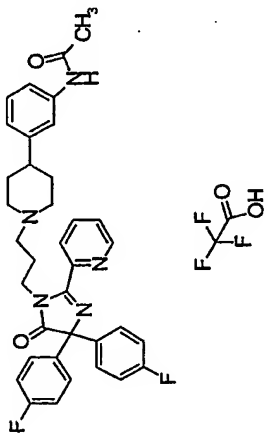
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
71		3-{3-[4-(1,3-benzodioxol-5-yl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2 & 19	532.40	2.45	
72		N-[3-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide trifluoroacetate	Example 2 & 19	545.10	2.31	
73		N-[3-(1-{3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide trifluoroacetate	Example 2 & 19	608.10	2.60	

Table 1

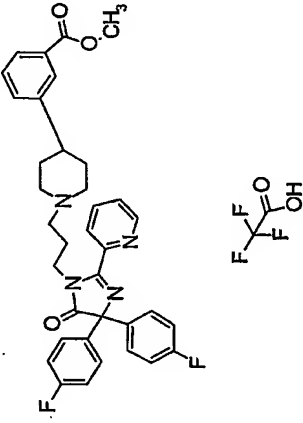
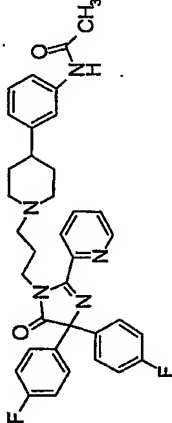
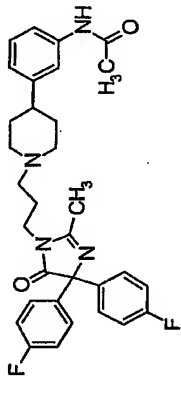
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
74		methyl 3-(1-{3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)benzoate trifluoroacetate	Example 2 & 19	613.10	2.45	
75		N-[3-(1-{3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide	Example 19	608.10	2.68	
76		N-[3-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide	Example 19	545.30	2.90	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
77		5,5-bis(4-fluorophenyl)-3-{3-[4-(2-methoxyphenyl)-1-piperidinyl]propyl}-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	581.10	2.93	
78		5,5-bis(4-fluorophenyl)-3-{3-[4-(2-methoxyphenyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	518.20	2.61	
79		3-{3-[4-(4-fluoro-2-methylphenyl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	583.10	2.99	
80		3-{3-[4-(4-fluoro-2-methylphenyl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	520.20	2.68	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
81		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-{3-[4-(2-pyrimidinyl)-1-piperazinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	554.10	2.61	
82		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(2-pyrimidinyl)-1-piperazinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	491.10	2.29	
83		3-{3-[4-(3-amino-4-fluorophenyl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	521.20	2.42	
84		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(4-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	489.30	1.70	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
85		3-{3-[4-(2,4-difluorophenyl)-1-piperazinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	525.10	2.56	
86		2-(4-{3-[4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-1-piperazinyl)benzonitrile	Example 2 & 19	514.10	2.47	
87		3-{3-[4-(3-chlorophenyl)-1-piperazinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	523.10	2.64	
88		3-{3-[4-(4-chlorophenyl)-1-piperazinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	523.10	2.61	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
89		3-{3-[4-(2,4-dimethylphenyl)-1-piperazinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	517.20	2.70	
90		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(trifluoromethyl)phenyl]-1-piperazinyl}propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2	557.10	2.72	
91		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(4-nitrophenyl)-1-piperazinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2	534.10	2.49	
92		5,5-bis(4-fluorophenyl)-3-{3-[4-(2-methoxyphenyl)-1-piperazinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	519.10	2.50	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
93		3-{3-[4-(4-acetylphenyl)-1-piperazinyl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	531.10	2.40	
94		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(4-pyridinyl)-1-piperazinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2	490.20	1.80	
95		3-{3-[5-(4-chlorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]propyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	535.10	2.62	
96		5,5-bis(4-fluorophenyl)-3-{3-[4-(2-methoxy-4-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	519.30	2.20	

Table 1

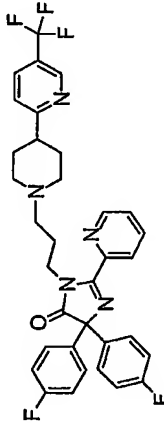
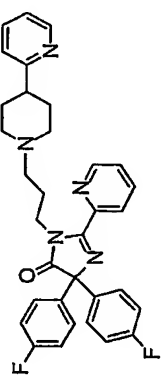
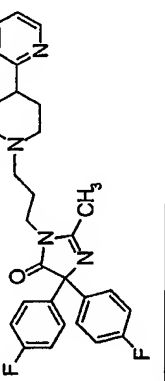
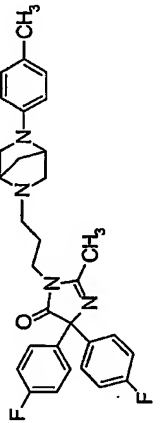
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
97		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-(3-[4-[5-(trifluoromethyl)-2-pyridinyl]-1-piperidinyl]propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	620.40	2.76	
98		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-(3-[4-(2-pyridinyl)-1-piperidinyl]propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	552.30	2.22	
99		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-[4-(2-pyridinyl)-1-piperidinyl]propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 19	489.30	1.94	
100		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-[5-(4-methylphenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	515.30	2.53	

Table 1

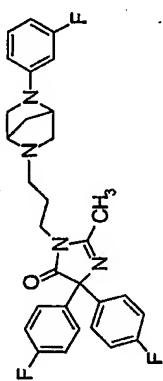
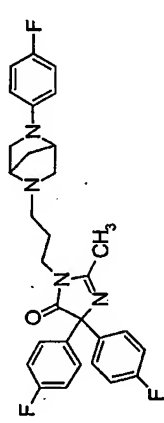
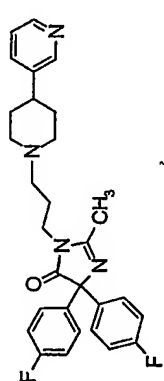
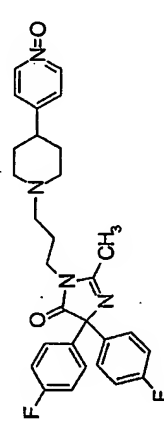
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
101		5,5-bis(4-fluorophenyl)-3-{3-[5-(3-fluorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one compound with 5-bis(4-fluorophenyl)-2-methyl-3-{3-[5-(4-methylphenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]propyl}-3,5-dihydro-4H-imidazol-4-one (1:1)	Example 2	519.30	2.47	
102		5,5-bis(4-fluorophenyl)-3-{3-[5-(4-fluorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one compound with 5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[5-(4-methylphenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]propyl}-3,5-dihydro-4H-imidazol-4-one (1:1)	Example 2	519.30	2.46	
103		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 16	489.10	1.98	
104		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(1-oxido-4-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2	505.30	1.80	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
105		4-(1-[3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl]-4-piperidinyl)-2-pyridinecarbonitrile	Example 2 & 16	514.10	0.77	
106		4-(1-[3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl]-4-piperidinyl)-N-(tert-butyl)-2-pyridinecarboxamide	Example 2 & 16	588.20	2.59	
107		methyl 4-(1-[3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl]-4-piperidinyl)-2-pyridinecarboxylate	Example 2 & 16	547.10	2.27	
108		methyl 4-(1-[3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl]-4-piperidinyl)-2-pyridinecarboxylate	Example 2 & 16	481.60	1.82	
109		5-ethyl-5-(4-fluorophenyl)-2-methyl-3-[3-[4-(3-pyridinyl)-1-piperidinyl]propyl]-3,5-dihydro-4H-imidazol-4-one	Example 2 & 16	423.20	0.91	

Table 1

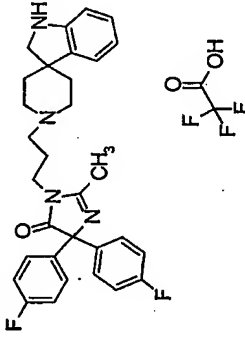
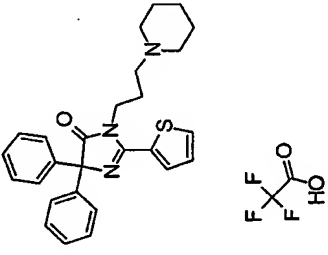
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
110		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-spiro[indoline-3,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 2	515.30	2.85	
111		5,5-diphenyl-3-[3-(1-piperidinyl)propyl]-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	444.20	2.38	

Table 1

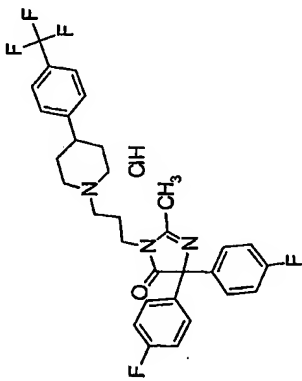
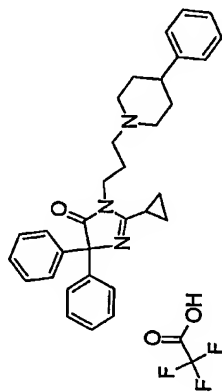
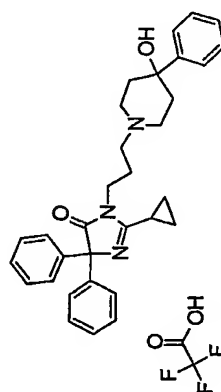
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
112		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-{4-[4-(trifluoromethyl)piperidinyl]phenyl}-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2	556.30	2.59	
113		2-cyclopropyl-5,5-diphenyl-3-[3-(4-phenyl-1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	478.30	2.56	
114		2-cyclopropyl-3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	494.30	2.42	

Table 1

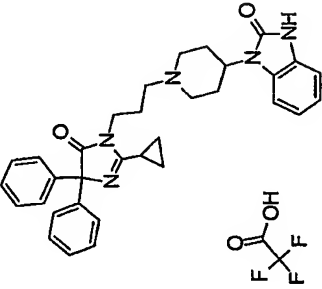
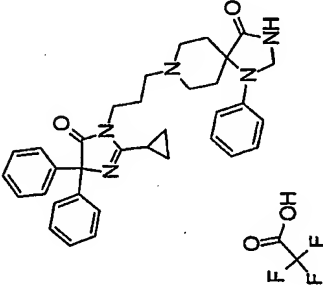
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
115		1-{1-[3-(2-cyclopropyl-5-oxo-4,4-diphenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-4-piperidyl}-1,3-dihydro-2H-benzimidazol-2-one trifluoroacetate	Example 2	534.20	2.33	
116		8-[3-(2-cyclopropyl-5-oxo-4,4-diphenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one trifluoroacetate	Example 2	548.30	2.40	

Table 1

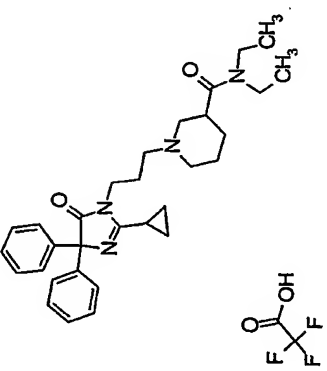
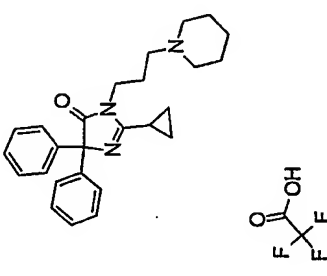
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
117		1-[3-(2-cyclopropyl-5-oxo-4,4-diphenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-N,N-diethyl-3-piperidinecarboxamide trifluoroacetate	Example 2	501.30	2.14	
118		2-cyclopropyl-5,5-diphenyl-3-[3-(1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	402.20	2.16	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
119		2-(4-methylphenyl)-5,5-diphenyl-3-[3-(4-phenyl-1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	528.30	2.62	
120		3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-2-(4-methylphenyl)-5,5-diphenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	544.30	2.46	
121		1-(1-[3-[2-(4-methylphenyl)-5-oxo-4,4-diphenyl-4,5-dihydro-1H-imidazol-1-yl]propyl]-4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one trifluoroacetate	Example 2	584.70	2.56	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
122		8-[3-[2-(4-methylphenyl)-5-oxo-4,4-diphenyl-4,5-dihydro-1H-imidazol-1-yl]propyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one trifluoroacetate	Example 2	598.30	2.54	
123		5,5-diphenyl-3-[3-(4-phenyl-1-piperidinyl)propyl]-2-(4-pyridinyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 3	515.30	2.39	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
124		3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-5,5-diphenyl-2-(4-pyridinyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 3	531.30	2.22	
125		1-(1-{3-[5-oxo-4,4-diphenyl-2-(4-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one bis(trifluoroacetate)	Example 3	571.20	2.22	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
126		8-{3-[5-oxo-4,4-diphenyl-2-(4-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one bis(trifluoroacetate)	Example 3	585.20	2.29	
127		2-cyclopropyl-5,5-diphenyl-3-{3-[4-(trifluoromethyl)phenyl]-1-piperazinyl}propyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	547.20	2.70	

Table 1

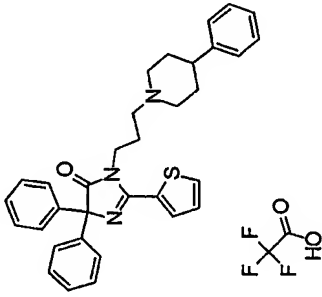
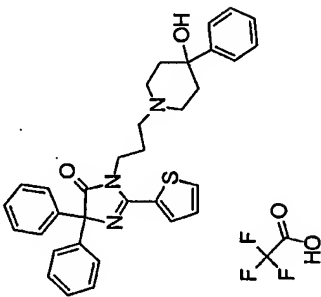
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
128		5,5-diphenyl-3-[3-(4-phenyl-1-piperidinyl)propyl]-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	520.20	2.73	
129		3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-5,5-diphenyl-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	536.10	2.66	

Table 1

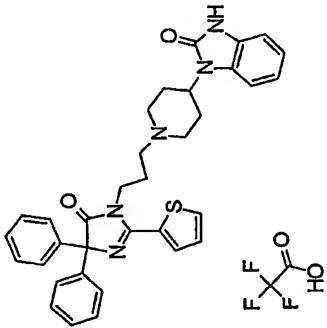
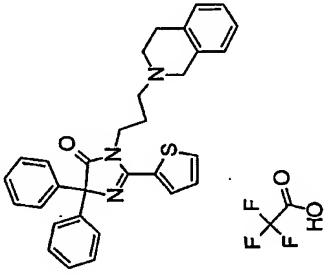
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130		1-(1-(3-[5-oxo-4,4-diphenyl-2-(2-thienyl)-4,5-dihydro-1H-imidazol-1-yl]propyl)-4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one trifluoroacetate	Example 3	576.10	2.52	
131		3-[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]-5,5-diphenyl-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	492.20	2.56	

Table 1

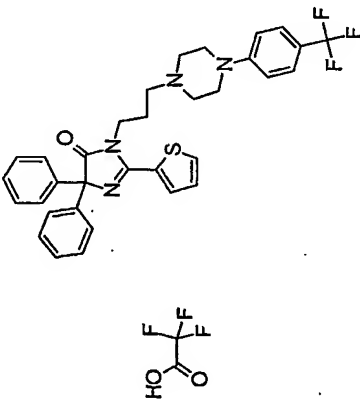
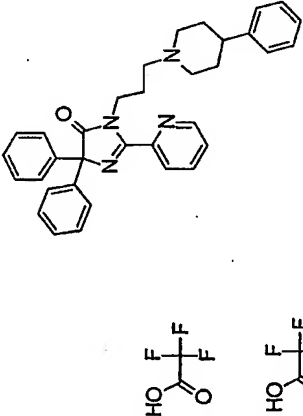
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
132		5,5-diphenyl-2-(2-thienyl)-3-(3-(4-(trifluoromethyl)phenyl)-1-piperazinyl)propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	589.10	2.89	
133		5,5-diphenyl-3-[3-(4-phenyl-1-piperidinyl)propyl]-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 3	515.30	2.64	

Table 1

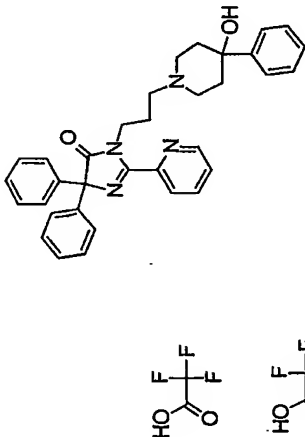
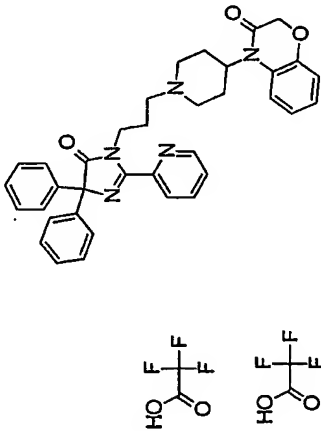
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
134		3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-5,5-diphenyl-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 3	531.20	2.46	
135		4-(1-{3-[5-oxo-4,4-diphenyl-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-2H-1,4-benzoxazin-3(4H)-one bis(trifluoroacetate)	Example 3	586.20	2.80	

Table 1

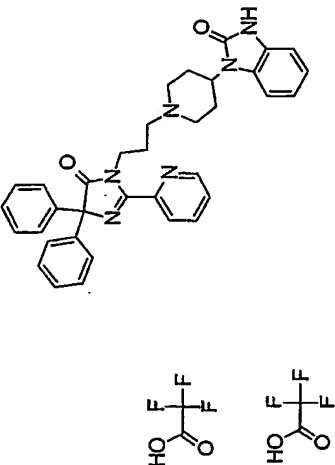
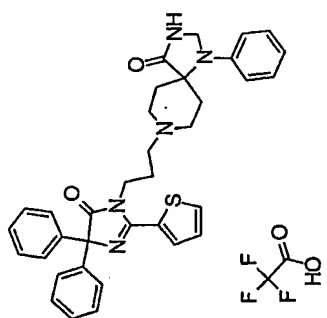
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
136		1-(1-{3-[5-oxo-4,4-diphenyl-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one bis(trifluoroacetate)	Example 3	571.30	2.43	
137		8-{3-[5-oxo-4,4-diphenyl-2-(2-thienyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one trifluoroacetate	Example 3	585.30	2.52	

Table 1

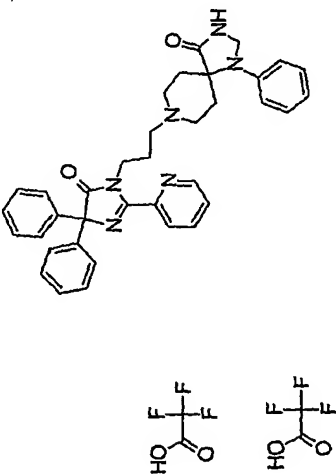
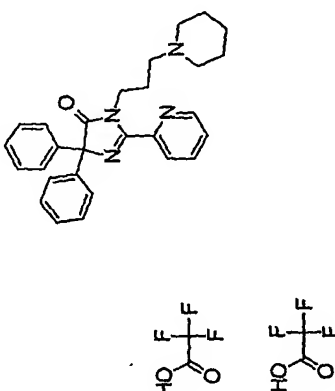
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
138		8-{3-[5-oxo-4,4-diphenyl-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one bis(trifluoroacetate)	Example 3	585.30	2.52	
139		5,5-diphenyl-3-[3-(1-piperidinyl)propyl]-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 3	439.30	2.80	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
140		3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-2-isopropyl-5-methyl-1H-imidazol-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	434.30	2.10	
141		4-{1-[3-(2-isopropyl-4-methyl-5-oxo-4-phenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-4-piperidinyl}-2H-1,4-benzoxazin-3(4H)-one trifluoroacetate	Example 2	489.20	2.12	
142		1-{1-[3-(2-isopropyl-4-methyl-5-oxo-4-phenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-4-piperidinyl}-1,3-dihydro-2H-benzimidazol-2-one trifluoroacetate	Example 2	474.30	1.95	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
143		3-[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]-2-isopropyl-5-methyl-5-phenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	390.30	1.93	
144		8-[3-(2-isopropyl-4-methyl-5-oxo-4-phenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one trifluoroacetate	Example 2	488.30	2.06	
145		2-isopropyl-5-methyl-5-phenyl-3-[3-(1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	342.30	40.00	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
146		2-isopropyl-5-methyl-3-(3-{4-[(trifluoromethyl)phenyl]-1-piperazinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	487.30	2.37	
147		2-isopropyl-5-methyl-3-[3-(4-morpholinyl)propyl]-5-phenyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	344.20	1.07	
148		2-isopropyl-5-methyl-3-[3-(4-methyl-1-piperazinyl)propyl]-5-phenyl-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 2	357.20	0.90	
149		2-isopropyl-5-methyl-3-(3-{4-(2-pyrimidinyl)-1-piperazinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	421.20	1.75	

Table 1

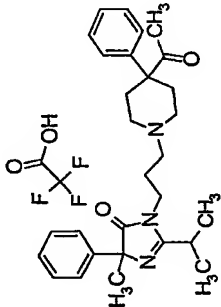
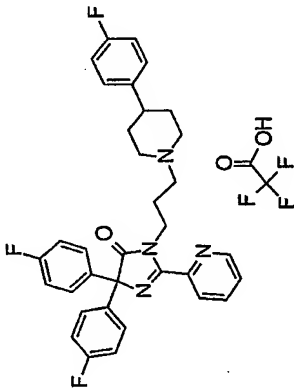
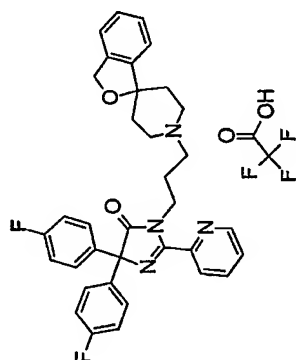
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
150		3-[3-(4-acetyl-4-phenyl-1-piperidinyl)propyl]-2-isopropyl-5-methyl-4H-imidazol-4-one trifluoroacetate	Example 2	460.30	2.12	
151		5,5-bis(4-fluorophenyl)-3-[3-[4-(4-fluorophenyl)-1-piperidinyl]propyl]-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	569.30	2.82	
152		5,5-bis(4-fluorophenyl)-2-pyridin-2-yl-3-[3-(1H,3H-spiro[2-benzofuran-1,4'-piperidin]-1'-yl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	579.40	2.80	

Table 1

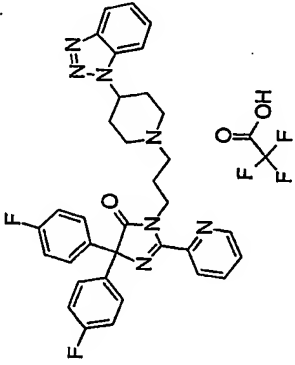
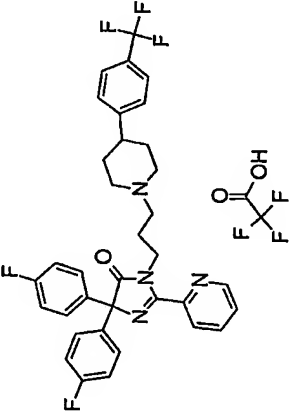
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
153		3-{3-[4-(1H-1,2,3-benzotriazol-1-yl)-1-piperidinyl]propyl}-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	592.30	2.63	
154		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-{3-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	619.30	2.98	

Table 1

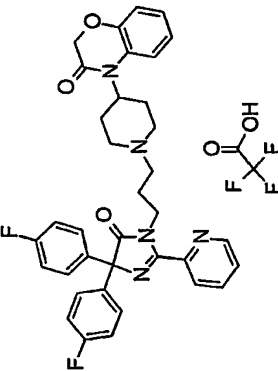
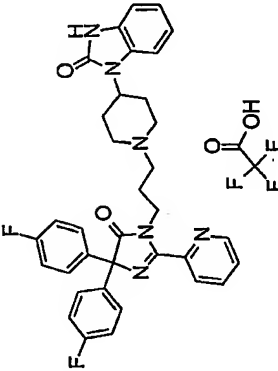
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
155		4-(1-(3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl)-4-piperidinyl)-2H-1,4-benzoxazin-3(4H)-one trifluoroacetate	Example 3	622.40	2.74	
156		1-(1-(3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl]propyl)-4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one trifluoroacetate	Example 3	607.40	2.60	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
157		5,5-bis(4-fluorophenyl)-3-[3-(4-hydroxy-4-phenyl-1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	490.20	2.24	
158		3-[3-(3,4-dihydro-2(1H)-isoquinolinyl)propyl]-5,5-bis(4-fluorophenyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	446.20	2.27	

Table 1

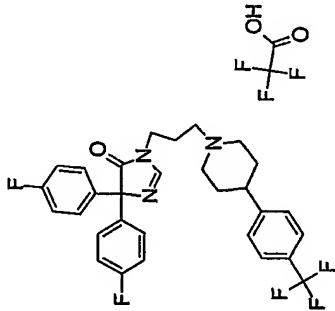
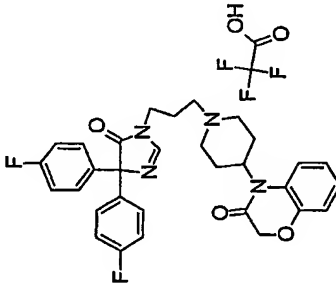
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
159		5,5-bis(4-fluorophenyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	542.20	2.65	
160		4-(1-{3-[4,4-bis(4-fluorophenyl)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-2H-1,4-benzoxazin-3(4H)-one trifluoroacetate	Example 2	545.20	2.40	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
161		1-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-1,3-dihydro-benzimidazol-2-one; compound with trifluoro-acetic acid	Example 2	530.20	2.24	
162		5,5-bis(4-fluorophenyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperazinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	543.10	2.59	

Table 1

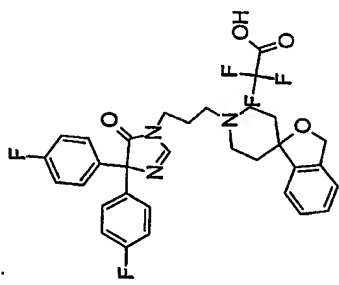
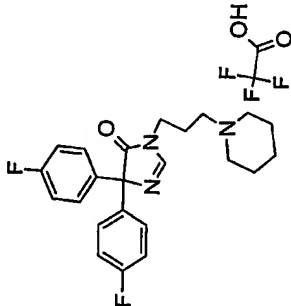
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
163		4,4-bis(4-fluorophenyl)-1-(3-(3,4-dihydroisobenzofuran-1,4'-piperidine)-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 2	502.30	2.42	
164		5,5-bis(4-fluorophenyl)-3-[3-(1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 2	398.30	2.03	

Table 1

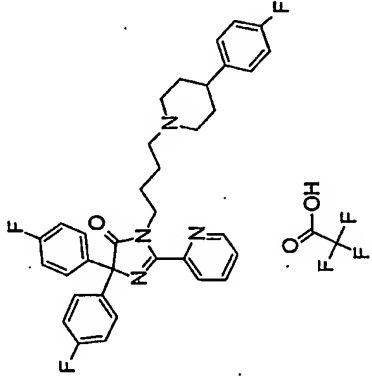
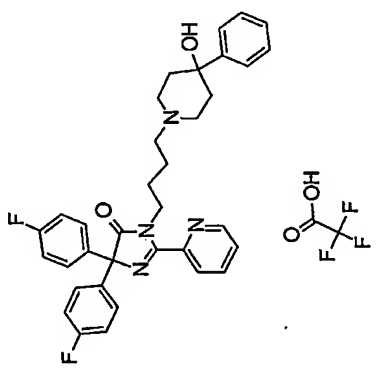
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
165		1-(1-(3-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl)-piperidin-4-yl)-1,3-dihydro-benzimidazol-2-one; compound with trifluoro-acetic acid	Example 3	583.40	2.72	
166		5,5-bis(4-fluorophenyl)-3-[4-(4-hydroxy-4-phenyl-1-piperidinyl)butyl]-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	581.40	2.50	

Table 1

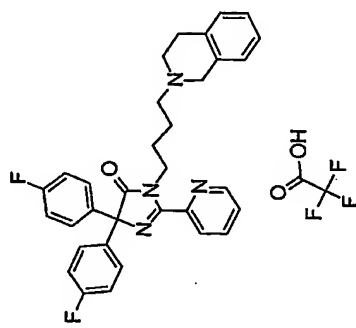
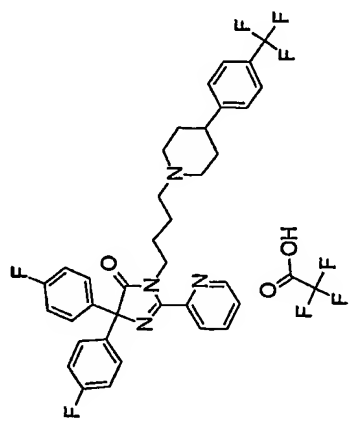
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
167		3-[4-(3,4-dihydro-2(1H)-isoquinolinyl)butyl]-5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	537.40	2.55	
168		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-(4-{4-(trifluoromethyl)phenyl}-1-piperidinyl)butyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	633.40	2.87	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
169		1-(1-(4-(4-bis(4-fluorophenyl)-5-oxo-2-(2-pyridinyl)-4,5-dihydro-1H-imidazol-1-yl)butyl)-4-piperidinyl)-1,3-dihydro-2H-benzimidazol-2-one trifluoroacetate	Example 3	621.50	2.49	
170		5,5-bis(4-fluorophenyl)-2-(2-pyridinyl)-3-(4-(4-(4-(trifluoromethyl)phenyl)-1-piperazinyl)butyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	634.40	2.85	

Table 1

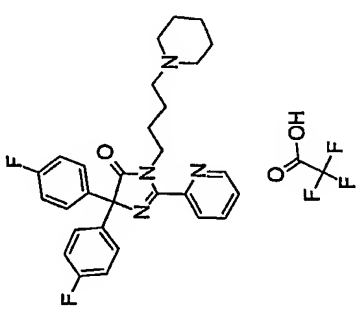
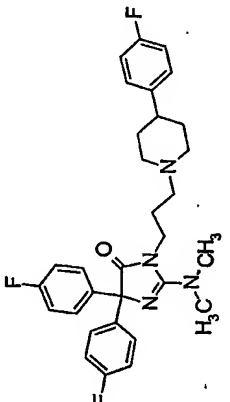
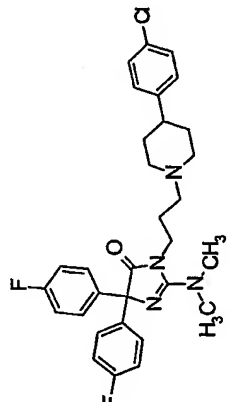
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
171		5,5-bis(4-fluorophenyl)-3-[4-(1-piperidinyl)butyl]-2-(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 3	489.40	2.39	
172		2-(dimethylamino)-5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2	535.20	2.28	
173		3-[3-[4-(4-chlorophenyl)-1-piperidinyl]propyl]-2-(dimethylamino)-5,5-bis(4-fluorophenyl)-3,5-dihydro-4H-imidazol-4-one	Example 2	551.10	2.36	

Table 1

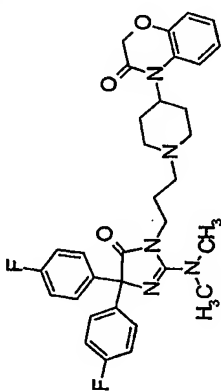
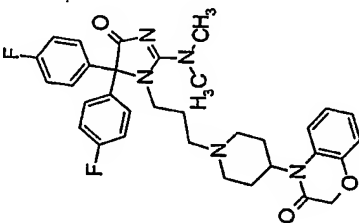
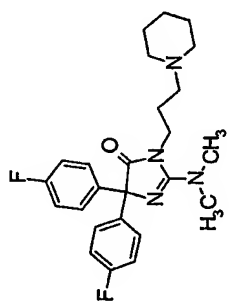
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
174		4-(1-{3-[2-(dimethylamino)-4,4-bis(4-fluorophenyl)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-2H-1,4-benzoxazin-3(4H)-one	Example 2	588.20	2.22	
175		4-(1-{3-[2-(dimethylamino)-5,5-bis(4-fluorophenyl)-4-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-2H-1,4-benzoxazin-3(4H)-one	Example 2	588.20	2.22	
176		2-(dimethylamino)-5,5-bis(4-fluorophenyl)-3-[3-(1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one	Example 2	441.20	1.89	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
177		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-(4-[3-(2-pyridinyl)-1,2,4-oxadiazol-5-yl]-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 24	557.30	2.94	
178		5,5-bis(4-fluorophenyl)-3-(3-(3-(4-hydroxy-4-(4-(trifluoromethyl)phenyl)-1-piperidinyl)propyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2	543.53	2.56	
179		5,5-bis(4-fluorophenyl)-3-(3-(3-(4-(2-hydroxyethyl)-1-piperidinyl)propyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2			

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
180		4,4-bis(4-fluorophenyl)-2-methyl-1-{3-[1-(methylsulfonyl)spiro[indoline-3,4'-piperidine]-10-yl]propyl}-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 2	593.30	3.01	
181		2-methyl-1-{3-[1-(methylsulfonyl)spiro[indoline-3,4'-piperidine]-10-yl]propyl}-4,4-diphenyl-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 2	557.30	2.97	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
182		5,5-Bis-(4-fluoro-phenyl)-2-methyl-3-{3-[4-(5-methyl-[1,3,4]oxadiazol-2-yl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 2 & 23	494.20	2.14	
183		3-{3-[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	534.10	2.46	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
184		3-[3-(4-Benzoyl-piperidin-1-yl)-propyl]-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	516.30	2.42	
185		3-[3-[4-(4-Chloro-benzoyl)-piperidin-1-yl]-propyl]-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	550.40	2.55	

Table 1

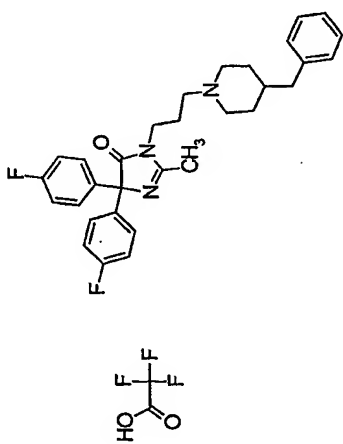
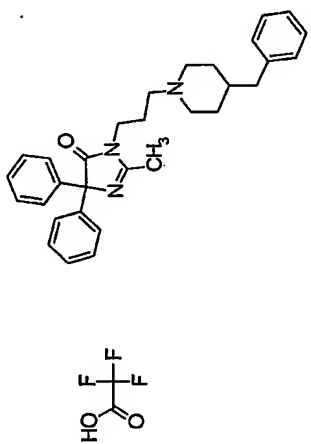
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
186		3-[3-(4-Benzyl-piperidin-1-yl)-propyl]-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	502.20	2.57	
187		3-[3-(4-Benzyl-piperidin-1-yl)-propyl]-2-methyl-5,5-diphenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	466.30	2.40	

Table 1

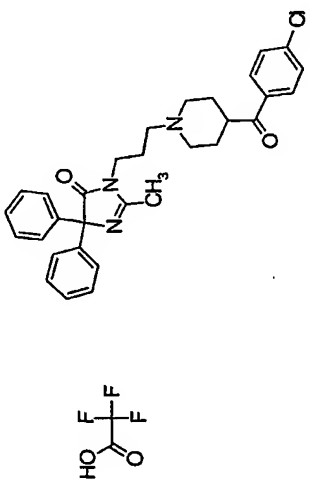
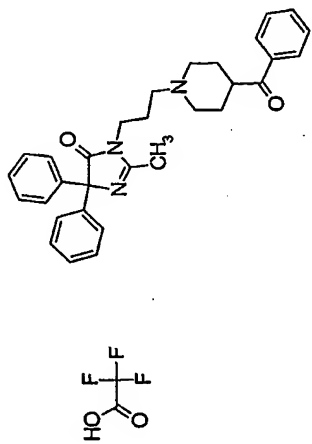
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
188		3-[3-[4-(4-Chloro-benzoyl)-piperidin-1-yl]-propyl]-2-methyl-5,5-diphenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	514.30	2.41	
189		3-[3-(4-Benzoyl-piperidin-1-yl)-propyl]-2-methyl-5,5-diphenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	480.30	2.26	

Table 1

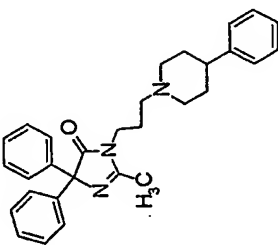
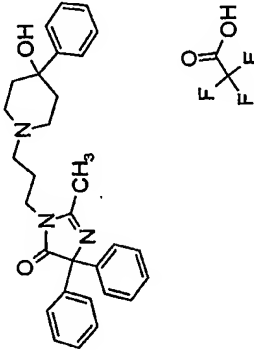
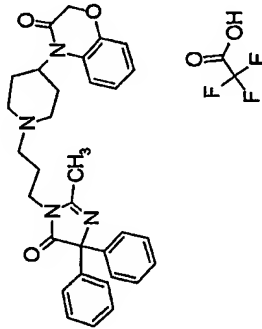
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
190		2-Methyl-5,5-diphenyl-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 2	452.30	2.25	
191		3-[3-(4-Hydroxy-4-phenyl-piperidin-1-yl)-propyl]-2-methyl-5,5-diphenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	468.30	2.13	
192		4-{1-[3-(2-Methyl-5-oxo-4,4-diphenyl-4,5-dihydro-imidazol-1-yl)-propyl]-piperidin-4-yl}-4H-benzol[1,4]oxazin-3-one; compound with trifluoro-acetic acid	Example 2	523.30	2.28	

Table 1

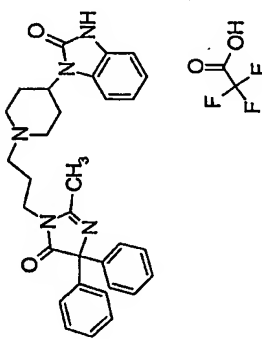
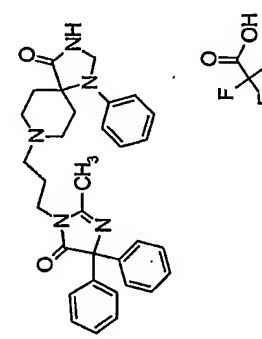
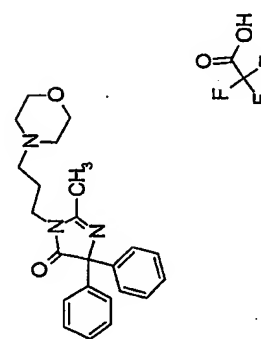
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
193		1-{1-[3-(2-Methyl-5-oxo-4,4-diphenyl-4,5-dihydroimidazol-1-yl)-propyl]-piperidin-4-yl}-1,3-dihydro-benzimidazol-2-one; compound with trifluoro-acetic acid	Example 2	508.20	2.13	
194		8-[3-(2-Methyl-5-oxo-4,4-diphenyl-4,5-dihydroimidazol-1-yl)-propyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one; compound with trifluoroacetic acid	Example 2	522.20	2.22	
195		2-Methyl-3-(3-morpholin-4-yl-propyl)-5,5-diphenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	378.20	1.79	

Table 1

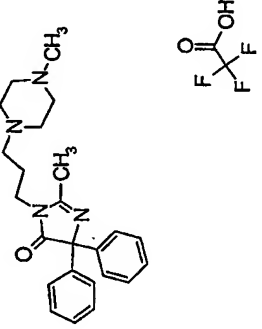
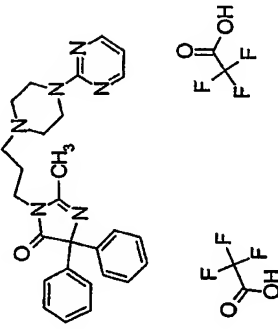
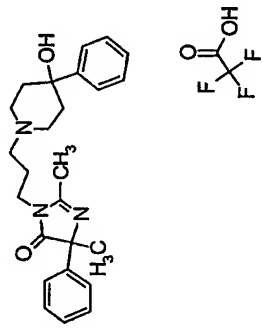
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
196		2-Methyl-3-[3-(4-methyl-piperazin-1-yl)-propyl]-5,5-diphenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	391.20	1.54	
197		2-methyl-5,5-diphenyl-3-[3-[4-(2-pyrimidinyl)-1-piperazinyl]propyl]-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 2	455.20	2.03	
198		3-[3-(4-Hydroxy-4-phenyl-piperidin-1-yl)-propyl]-2,5-dimethyl-5-phenyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 5	406.10	1.57	

Table 1

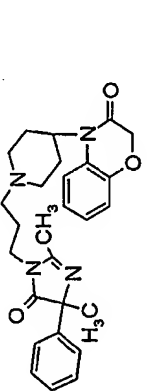
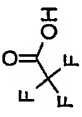
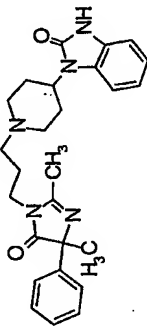

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
199	 	4-{1-[3-(2,4-Dimethyl-5-oxo-4-phenyl-4,5-dihydro-imidazol-1-yl)-propyl]-piperidin-4-yl}-4H-benzol[1,4]oxazin-3-one; compound with trifluoro-acetic acid	Example 5	461.10	1.89	
200	 	1-{1-[3-(2,4-Dimethyl-5-oxo-4-phenyl-4,5-dihydro-imidazol-1-yl)-propyl]-piperidin-4-yl}-1,3-dihydro-benzimidazol-2-one; compound with trifluoro-acetic acid	Example 5	446.10	1.69	

Table 1

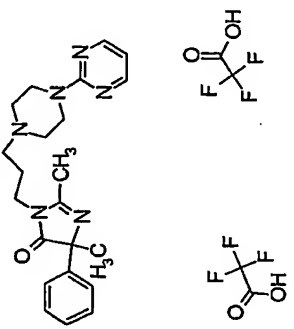
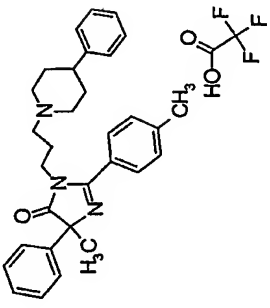
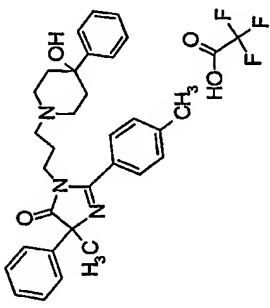
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
201		2,5-dimethyl-5-phenyl-3-[3-[4-(2-pyrimidinyl)-1-piperazinyl]propyl]-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 5	393.10	0.68	
202		5-Methyl-5-phenyl-3-[3-(4-phenyl-piperidin-1-yl)propyl]-2-p-tolyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 5	466.30	2.41	
203		3-[3-(4-Hydroxy-4-phenyl-piperidin-1-yl)-propyl]-5-methyl-5-phenyl-2-p-tolyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 5	482.20	2.22	

Table 1

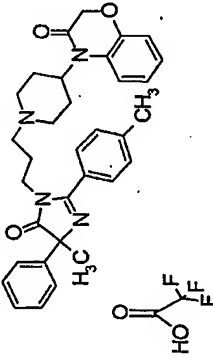
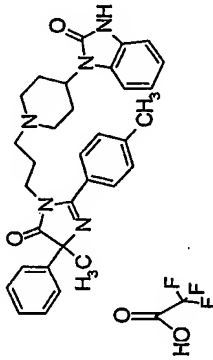
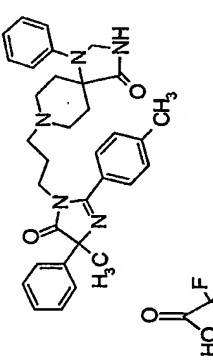
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
204		4-{1-[3-(4-Methyl-5-oxo-4-phenyl-2-p-tolyl-4,5-dihydroimidazol-1-yl)-propyl]-piperidin-4-yl}-4H-benzo[1,4]oxazin-3-one; compound with trifluoro-acetic acid	Example 5	537.20	2.30	
205		1-{1-[3-(4-Methyl-5-oxo-4-phenyl-2-p-tolyl-4,5-dihydroimidazol-1-yl)-propyl]-piperidin-4-yl}-1,3-dihydro-benzolimidazol-2-one; compound with trifluoro-acetic acid	Example 5	522.20	2.18	
206		3-[3-(3,4-Dihydro-1H-isoquinolin-2-yl)-propyl]-5-methyl-5-phenyl-2-p-tolyl-3,5-dihydroimidazol-4-one; compound with trifluoro-acetic acid	Example 5	536.30	2.27	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
207		3-{3-(3,4-Dihydro-1H-isoquinolin-2-yl)-propyl}-5-methyl-5-phenyl-2-p-tolyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 5	438.20	2.21	
208		5-Methyl-5-phenyl-3-(3-piperidin-1-yl-propyl)-2-p-tolyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 5	390.20	1.97	
209		5-methyl-2-(4-methylphenyl)-5-phenyl-3-(3-{4-[4-(trifluoromethyl)phenyl]phenyl}-1-piperazinyl)propyl}-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 5	535.20	2.57	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
210		5-Methyl-3-(3-morpholin-4-yl-propyl)-5-phenyl-2-p-tolyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 5	392.20	1.86	
211		5-methyl-2-(4-methylphenyl)-3-[3-(4-methyl-1-piperazinyl)propyl]-5-phenyl-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 5	405.20	1.71	
212		5-methyl-2-(4-methylphenyl)-5-phenyl-3-[3-(4-(2-pyrimidinyl)-1-piperazinyl)propyl]-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 5	469.20	2.08	

Table 1

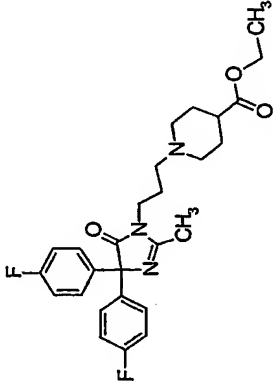
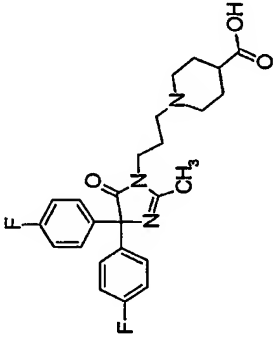
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
213		1-(3-{4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl}-propyl)-piperidine-4-carboxylic acid ethyl ester	Example 22	484.30	2.20	
214		1-(3-{4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl}-propyl)-piperidine-4-carboxylic acid	Example 22	456.20	2.05	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
215		3-{3-[4-(3-Ethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 24	508.40	2.28	
216		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(3-methoxymethyl-[1,2,4]oxadiazol-5-yl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 24	524.40	2.05	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
217		3-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-3-oxo-propionic acid ethyl ester	Example 22	526.30	2.95	
218		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(6-hydroxy-2-methyl-pyrimidin-4-yl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 22	520.20	2.75	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
219		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(6-hydroxy-2-isopropyl-pyrimidin-4-yl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 22	548.30	2.20	
220		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(6-hydroxy-2-isopropyl-pyrimidin-4-yl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 22	506.20	1.98	

Table 1

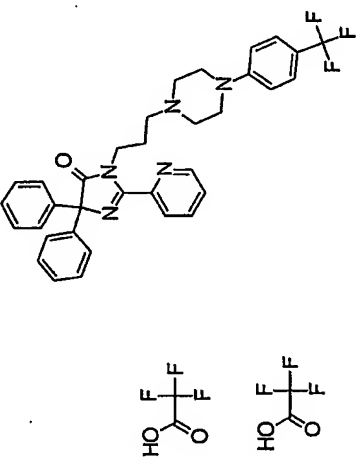
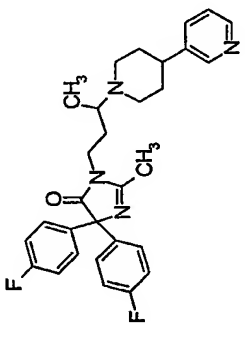
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
221		5,5-diphenyl-2-(2-pyridinyl)-3-(3-(4-(4-(trifluoromethyl)phenyl)-1-piperazinyl)propyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 3	584.30	2.80	
222		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-(4-(3-pyridinyl)-1-piperidinyl)butyl)-3,5-dihydro-4H-imidazol-4-one	Example 4	503.10	1.94	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
223		methyl 4-(1-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]-1-methylpiperidin}-2-pyridinyl)-2-pyridinecarboxylate	Example 4	561.10	2.33	
224		2-(4-fluorophenyl)-5,5-di(2-pyridinyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one	Example 1 & 10	602.10	2.44	
225		2-(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]propyl}-5,5-di(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 1 & 10	552.10	2.24	

Table 1

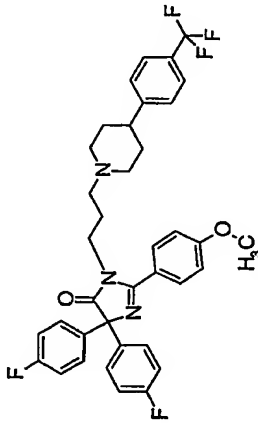
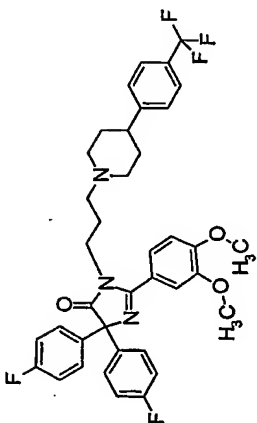
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
226		5,5-bis(4-fluorophenyl)-2-(4-methoxyphenyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]phenyl}-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1 & 10	648.50	2.92	
227		2-(3,4-dimethoxyphenyl)-5,5-bis(4-fluorophenyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]phenyl}-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1 & 10	678.50	2.88	

Table 1

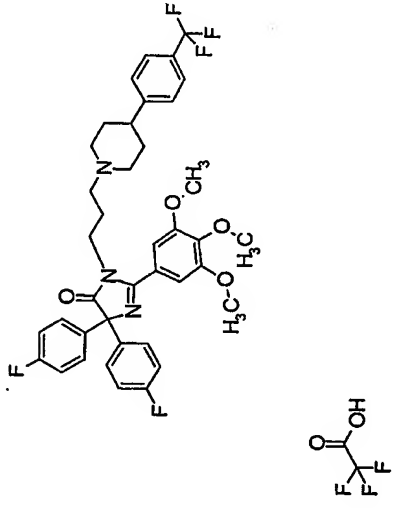
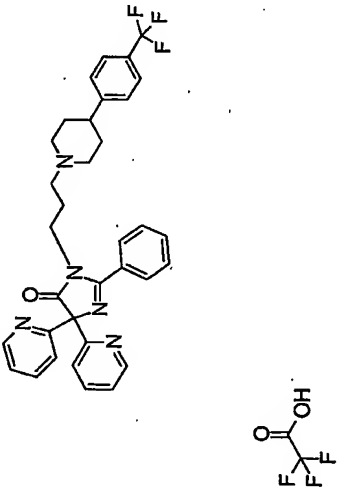
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
228		5,5-bis(4-fluorophenyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-2-(3,4,5-trimethoxyphenyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1 & 10	708.20	3.09	
229		2-phenyl-5,5-di(2-pyridinyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1 & 10	584.60	2.28	

Table 1

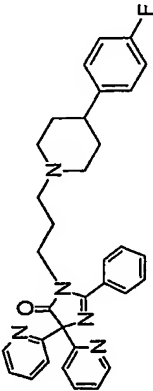
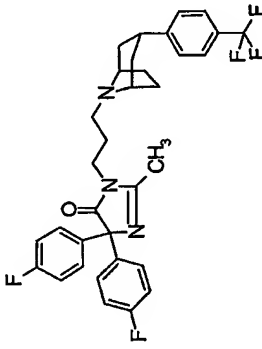
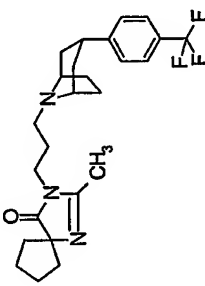
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
230		3-(3-[4-(4-fluorophenyl)-1-piperidinyl]propyl)-2-phenyl-5,5-di(2-pyridinyl)-3,5-dihydro-4H-imidazol-4-one	Example 1 & 10	534.10	2.20	
231		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-[4-(trifluoromethyl)phenyl]-8-azabicyclo[3.2.1]oct-8-yl)propyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 18	582.50	2.69	
232		2-methyl-3-(3-[4-(trifluoromethyl)phenyl]-8-azabicyclo[3.2.1]oct-8-yl)propyl)-1,3-diazaspiro[4.4]non-1-en-4-one	Example 2 & 18	448.30	1.98	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
233		5,5-bis(4-fluorophenyl)-2-[(2-methoxyethyl)amino]-3-[(4-{(trifluoromethyl)phenyl}-1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	615.30	2.37	
234		5,5-bis(4-fluorophenyl)-2-[(2-methoxyethyl)(methyl)amino]-3-[(4-{(trifluoromethyl)phenyl}-1-piperidinyl)propyl]-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	629.30	3.17	

Table 1

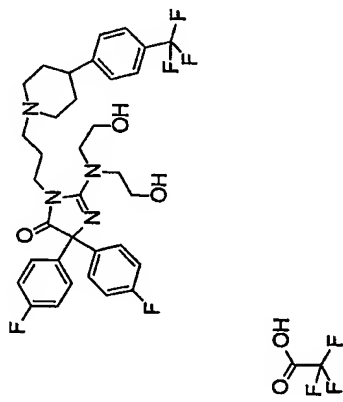
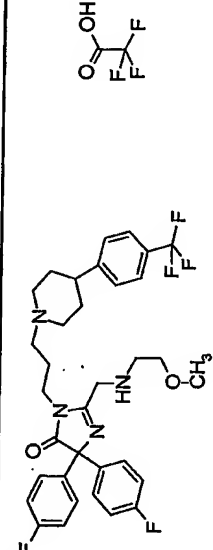
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
235		2-[[bis(2-hydroxyethyl)amino]-5,5-bis(4-fluorophenyl)-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	645.40	3.21	
236		5,5-bis(4-fluorophenyl)-2-[[2-methoxyethyl)amino]methyl]-3-(3-{4-[4-(trifluoromethyl)phenyl]-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	629.30	3.19	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
237		5,5-bis(4-fluorophenyl)-2-(((2-methoxyethyl)(methyl)amino)methyl)-3-(3-(4-(trifluoromethyl)phenyl)-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	643.40	2.46	
238		5,5-bis(4-fluorophenyl)-2-(((2-hydroxyethyl)(methyl)amino)methyl)-3-(3-(4-(trifluoromethyl)phenyl)-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	629.30	2.46	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
239		2-allyl-5,5-bis(4-fluorophenyl)-3-(3-{4-(trifluoromethyl)phenyl}-1-piperidinyl)propyl)-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	582.20	3.55	
240		methyl 4-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]-2-[4-(trifluoromethyl)phenyl]-1-piperidinyl]butanoate	Example 2	614.20	2.88	
241		5,5-bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 4	520.20	2.65	

Table 1

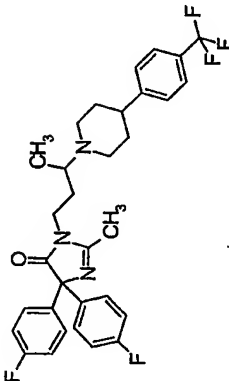
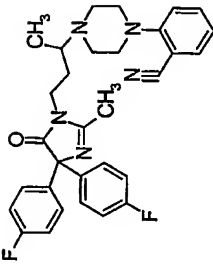
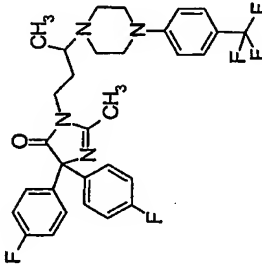
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
242		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-(4-[4-(trifluoromethyl)phenyl]-1-piperidinyl)butyl)-3,5-dihydro-4H-imidazol-4-one	Example 4	570.10	2.83	
243		2-(4-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]-1-methylpropyl}-1-piperazinyl)benzonitrile	Example 4	528.10	2.57	
244		5,5-bis(4-fluorophenyl)-2-methyl-3-(3-(4-[4-(trifluoromethyl)phenyl]-1-piperazinyl)butyl)-3,5-dihydro-4H-imidazol-4-one	Example 4	571.10	2.82	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
245		5,5-bis(4-fluorophenyl)-3-[3-[4-(4-fluorophenyl)-1-piperazinyl]butyl]-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 4	521.20	2.46	
246		5,5-bis(4-fluorophenyl)-2-methyl-3-[3-[4-(4-(4-fluorophenyl)-1-piperazinyl]butyl)-3,5-dihydro-4H-imidazol-4-one	Example 4	504.20	1.94	
247		5,5-bis(4-fluorophenyl)-2-methyl-3-[3-(4-phenyl-1-piperazinyl)butyl]-3,5-dihydro-4H-imidazol-4-one	Example 4	503.10	2.56	

Table 1

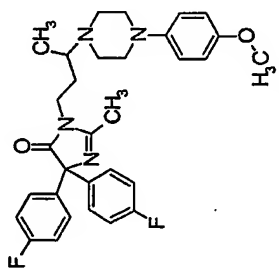
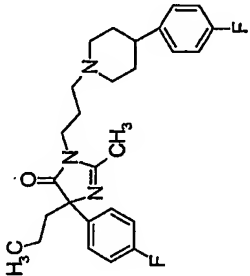
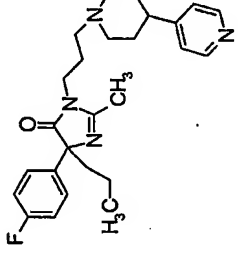
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
248		5,5-bis(4-fluorophenyl)-3-{3-[4-(4-methoxyphenyl)-1-piperazinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 4	533.10	2.60	
249		5-(4-Fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-methyl-5-propyl-3,5-dihydro-imidazol-4-one	Example 2 & 8	454.20	2.34	
250		5-(4-Fluoro-phenyl)-2-methyl-5-propyl-3-{3-(3,4,5,6-tetrahydro-2H-[4,4'-bipyridinyl]-1-yl)-propyl}-3,5-dihydro-imidazol-4-one	Example 2 & 8	437.20	1.43	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
251		N-[3-(1-{3-[4-(4-Fluoro-phenyl)-2-methyl-5-oxo-4-propyl-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-phenyl]-acetamide	Example 2 & 8	493.20	2.16	
252		5,5-Bis-(4-fluoro-phenyl)-2-methyl-3-[3-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-butyl]-3,5-dihydro-imidazol-4-one	Example 4	503.10	1.91	
253		4-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-2-[4-(4-fluoro-phenyl)-piperidin-1-yl]-butyric acid methyl ester	Example 4	564.20	2.75	

Table 1

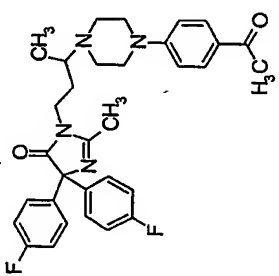
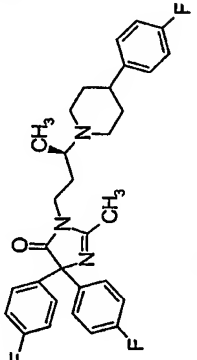
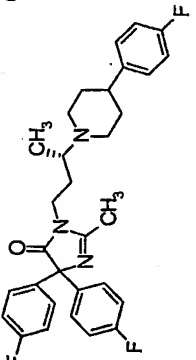
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
254		3-{3-[4-(4-Acetyl-phenyl)-piperazin-1-yl]-butyl}- 5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro- imidazol-4-one	Example 4	545.10	2.47	
255		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro- phenyl)-piperidin-1-yl]-butyl}-2-methyl-3,5- dihydro-imidazol-4-one	Example 4	520.10	2.55	
256		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro- phenyl)-piperidin-1-yl]-butyl}-2-methyl-3,5- dihydro-imidazol-4-one	Example 4	520.20	2.57	

Table 1

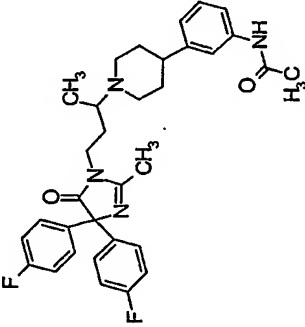
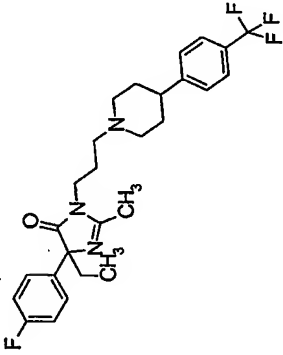
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
257		N-[3-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-1-methyl-propyl]-piperidin-4-yl)-phenyl]-acetamide	Example 4	559.20	2.43	
258		5-Ethyl-5-(4-(4-fluoro-phenyl)-2-methyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 5 & 8	490.20	2.48	0.25 CH ₂ Cl ₂ : MeOH 9:1

Table 1

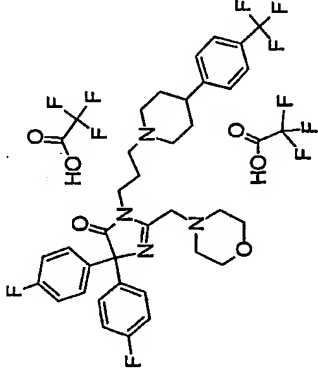
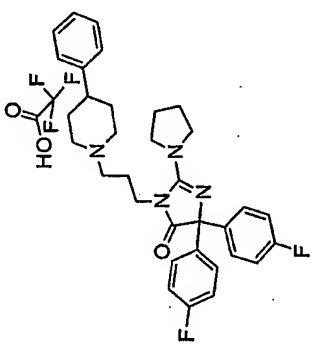
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
259		5,5-Bis-(4-fluorophenyl)-2-(morpholin-4-ylmethyl)-3-(3-{4-[(trifluoromethyl)phenyl]piperidin-1-yl}propyl)-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 2 & 11	641.30	3.28	0.35 CH ₂ Cl ₂ : MeOH 9:1
260		5,5-Bis-(4-fluoro-phenyl)-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-2-pyrrolidin-1-yl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	543.30	2.88	0.20 CH ₂ Cl ₂ : MeOH 9:1

Table 1

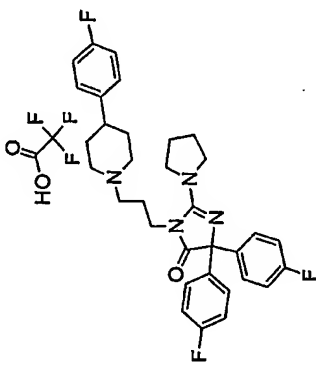
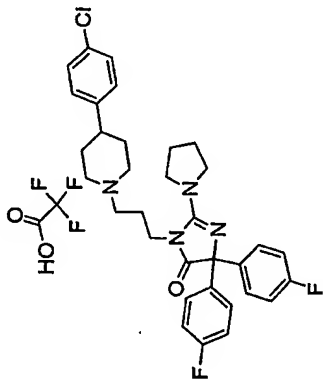
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
261		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-pyrrolidin-1-yl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	561.30	3.04	0.25 CH ₂ Cl ₂ : MeOH 9:1
262		3-{3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-pyrrolidin-1-yl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	577.30	3.11	0.25 CH ₂ Cl ₂ : MeOH 9:1

Table 1

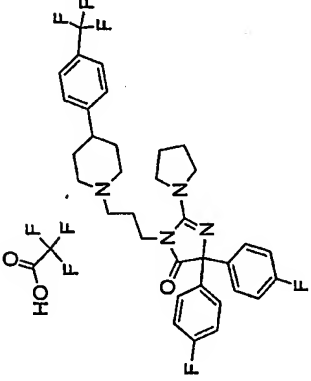
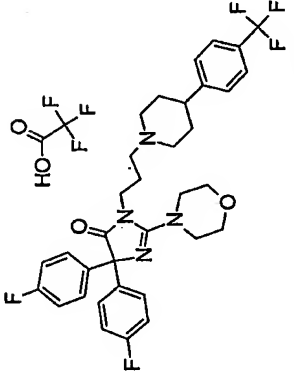
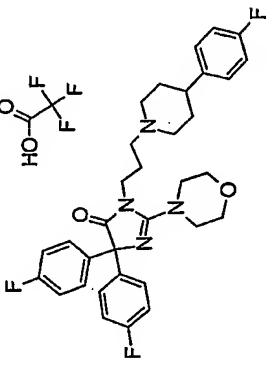
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
263		5,5-Bis-(4-fluoro-phenyl)-2-pyrrolidin-1-yl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	611.30	3.07	0.15 CH ₂ Cl ₂ : MeOH 9:1
264		5,5-Bis-(4-fluoro-phenyl)-2-morpholin-4-yl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	627.30	2.53	0.20 CH ₂ Cl ₂ : MeOH 9:1
265		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-morpholin-4-yl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	577.20	2.42	0.20 CH ₂ Cl ₂ : MeOH 9:1

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
266		3-{3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-morpholin-4-yl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	593.30	2.45	0.20 CH ₂ Cl ₂ : MeOH 9:1
267		5,5-Bis-(4-fluoro-phenyl)-2-morpholin-4-ylmethyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 2 & 11	641.10	2.65	0.20 CH ₂ Cl ₂ : MeOH 9:1
268		3-{3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-morpholin-4-yl-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 15	570.40	3.56	0.20 EtOAc/Hex 1:1

Table 1

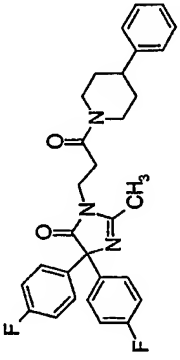
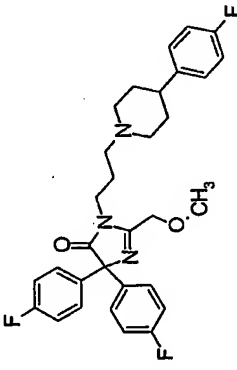
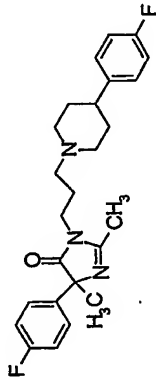
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
269		5,5-Bis-(4-fluoro-phenyl)-2-morpholin-4-ylmethyl-3-[4-(4-trifluoromethyl)-phenyl]-piperidin-1-yl-propyl-3,5-dihydro-imidazol-4-one	Example 15	502.40	3.32	0.15 EtOAc/Hex 1:1
270		5,5-Bis-(4-fluoro-phenyl)-3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl-2-methoxymethyl-3,5-dihydro-imidazol-4-one	Example 2 & 10	536.10	2.64	0.15 CH ₂ Cl ₂ : MeOH 9:1
271		5-(4-Fluoro-phenyl)-3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl-2,5-dimethyl-3,5-dihydro-imidazol-4-one	Example 2 & 8	426.20	2.16	0.20 CH ₂ Cl ₂ : MeOH 9:1

Table 1

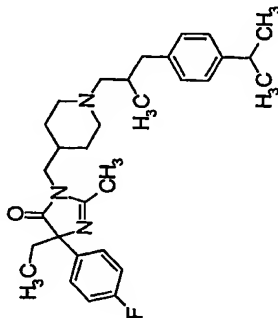
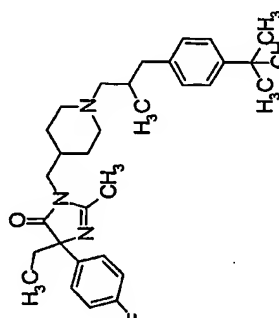
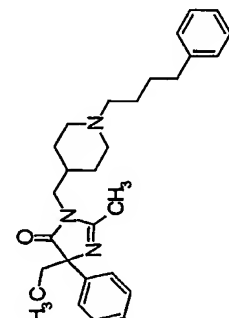
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
272		5-Ethyl-5-(4-fluoro-phenyl)-3-{1-[3-(4-isopropyl-phenyl)-2-methyl-propyl]-piperidin-4-ylmethyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 8 & 14	492.50	2.50	0.20 CH ₂ Cl ₂ : MeOH 9:1
273		3-{1-[3-(4-tert-Butyl-phenyl)-2-methyl-propyl]-piperidin-4-ylmethyl}-5-ethyl-5-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 8 & 14	506.60	2.60	0.20 CH ₂ Cl ₂ : MeOH 9:1
274		5-Ethyl-5-(4-fluoro-phenyl)-2-methyl-3-[1-(4-phenyl-butyl)-piperidin-4-ylmethyl]-3,5-dihydro-imidazol-4-one	Example 8 & 14	450.50	2.19	0.26 CH ₂ Cl ₂ : MeOH 9:1

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
275		5-Ethyl-5-(4-fluoro-phenyl)-2-methyl-3-[1-(3-phenyl-propyl)-piperidin-4-ylmethyl]-3,5-dihydroimidazol-4-one	Example 8 & 14	436.50	2.13	0.40 CH ₂ Cl ₂ : MeOH 9:1
276		5,5-Diethyl-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-3,5-dihydroimidazol-4-one	Example 2	436.40	2.05	0.55 CH ₂ Cl ₂ : MeOH 9:1
277		5-Ethyl-5-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydroimidazol-4-one	Example 5	440.40	2.15	0.44 CH ₂ Cl ₂ : MeOH 9:1

Table 1

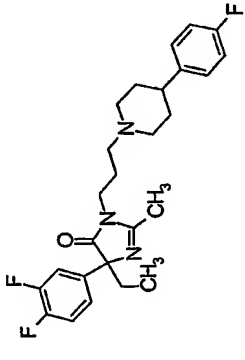
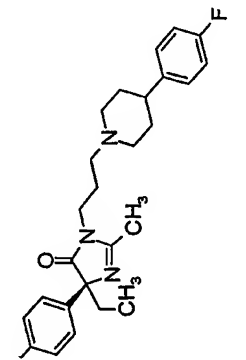
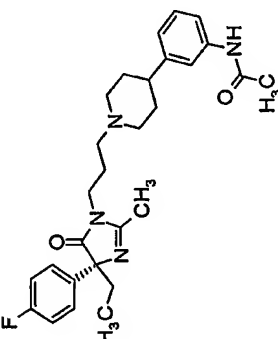
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
278		5-(3,4-Difluoro-phenyl)-5-ethyl-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 2 & 8	458.40	2.23	0.53 CH ₂ Cl ₂ : MeOH 9:1
279		5-Ethyl-5-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 5	440.40	2.15	0.60 CH ₂ Cl ₂ : MeOH 9:1
280		N-[3-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-phenyl]-acetamide	Example 5 & 16	479.20	1.98	0.19 4% MeOH/ 1% NH ₄ OH/ 95% CH ₂ Cl ₂

Table 1

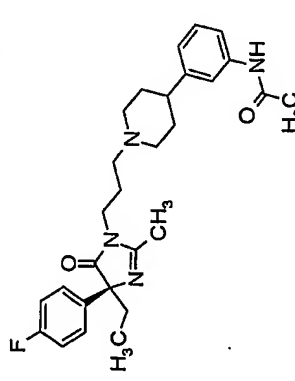
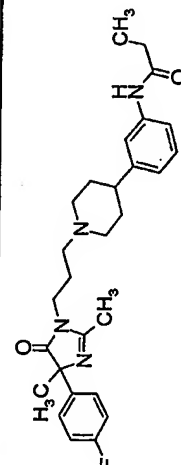
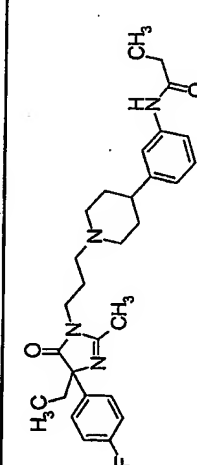
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
281		N-[3-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-phenyl]-acetamide	Example 5 & 16	479.40	1.98	0.19 4% MeOH/ 1%NH ₄ OH/ 95%CH ₂ Cl ₂
282		N-[3-(1-{3-[4-(4-Fluoro-phenyl)-2,4-dimethyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-phenyl]-propionamide	Example 8 & 16	479.20	1.99	0.58 CHCl ₃ : MeOH: NH ₄ OH 8:1.5:0.5
283		N-[3-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-phenyl]-propionamide	Example 8 & 16	493.20	2.06	0.65 CHCl ₃ : MeOH: NH ₄ OH 8:1.5:0.5

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
284		N-[3-(1-{3-[4-(4-Fluoro-phenyl)-2,4-dimethyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-phenyl]-isobutyramide	Example 8 & 16	493.20	2.05	0.55 CHCl ₃ : MeOH: NH ₄ OH 9:1.0:0.5
285		N-[3-(1-{3-[4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-phenyl]-isobutyramide	Example 8 & 16	507.20	2.14	0.62 CHCl ₃ : MeOH: NH ₄ OH 9:1.0:0.5
286		2-Ethyl-5,5-bis-(4-fluoro-phenyl)-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	570.20		0.09 100% EtOAc

Table 1

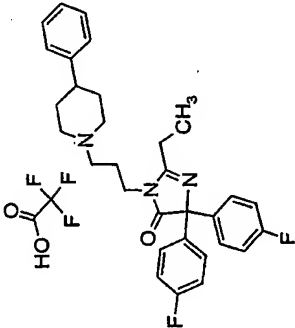
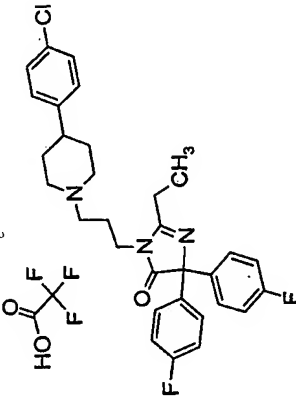
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
287		2-Ethyl-5,5-bis-(4-fluoro-phenyl)-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	502.20	2.61	0.09 EtOAc
288		3-[3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-propyl]-2-ethyl-5,5-bis-(4-fluoro-phenyl)-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 2	536.20	2.74	0.07 EtOAc

Table 1

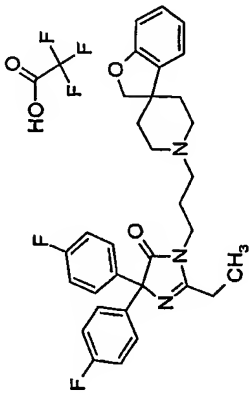
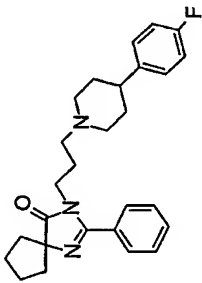
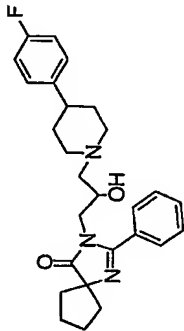
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
289		4,4-bis(4-fluorophenyl)-2-ethyl-1-(3-spiro[2,3-dihydrobenzo[b]furan-3,4'-piperidin]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 2	530.20	2.68	0.43 MeOH:EtOAc 2:8
290		3-{3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-1,3-diaza-spiro[4.4]non-1-en-4-one	Example 2	434.40	1.94	0.12 MeOH/CH2Cl2 0.05:1
291		3-{3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-phenyl-1,3-diaza-spiro[4.4]non-1-en-4-one	Example 2 & 6	450.20	1.99	0.25 CH2Cl2:MeOH 9.5:0.5

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
292		3-{2-Hydroxy-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-1,3-diazaspiro[4.4]non-1-en-4-one	Example 2 & 6	500.40	2.14	0.27 CH ₂ Cl ₂ :MeOH 9.5:0.5
293		3-{2-Hydroxy-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-methyl-1,3-diazaspiro[4.4]non-1-en-4-one	Example 2 & 6	438.30	1.77	0.07 CH ₂ Cl ₂ :MeOH 9.5:0.5
294		3-{3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-propyl}-2-methyl-1,3-diazaspiro[4.4]non-1-en-4-one	Example 2	372.20	1.45	0.13 CH ₂ Cl ₂ :MeOH 9.5:0.5
295		2-Phenyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-1,3-diazaspiro[4.4]non-1-en-4-one	Example 2	484.40	2.21	0.10 CH ₂ Cl ₂ :MeOH 9.5:0.5

Table 1

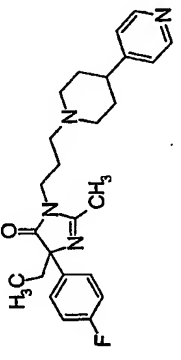
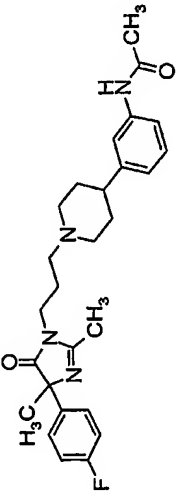
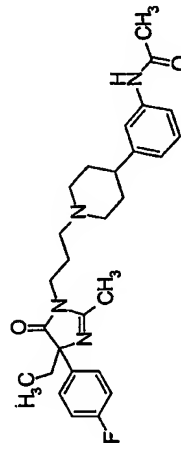
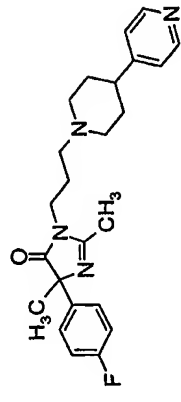
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
296		5-Ethyl-5-(4-fluoro-phenyl)-2-methyl-3-[3-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 8 & 19	423.20	0.71	0.17 CH ₂ Cl ₂ :MeOH 9.5:0.5
297		N-[3-(1-{3-[4-(4-Fluoro-phenyl)-2,4-dimethyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-phenyl]-acetamide	Example 8 & 16	465.40	1.81	0.16 CH ₂ Cl ₂ :MeOH :NH ₄ OH 9.0:0.75:0.25
298		N-[3-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-phenyl]-acetamide	Example 8 & 16	479.20	1.97	0.16 CH ₂ Cl ₂ :MeOH :NH ₄ OH 9.0:0.75:0.25
299		5-Ethyl-5-(4-fluoro-phenyl)-3-[3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 5 & 8	440.40	2.15	0.60 CH ₂ Cl ₂ :MeOH 9:1

Table 1

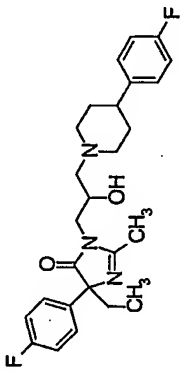
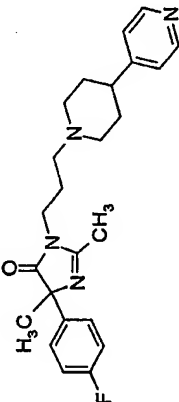
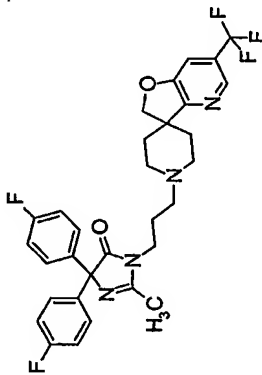
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
300		5-Ethyl-5-(4-fluoro-phenyl)-3-[3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 6 & 8	456.40	2.10	0.12 EtOAc:Hex: MeOH 5:4:5:0.5
301		5-(4-Fluoro-phenyl)-2,5-dimethyl-3-[3-(3,4,5,6-tetrahydro-2H-[4,4']bipyridinyl-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 8 & 19	409.20	0.72	0.17 CH ₂ Cl ₂ :MeOH 9:5:0.5
302		3-[3-[6-trifluoromethyl-spiro(2,3-dihydro-4-pyridinofuran-3,4'-piperidin)-1'-yl]propyl]-5,5-di(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 25 & 30	585.00	2.26	0.19 EtOAc:Hex: MeOH 6:3:1

Table 1

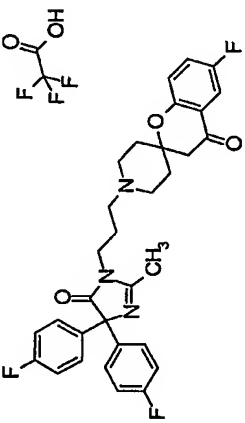
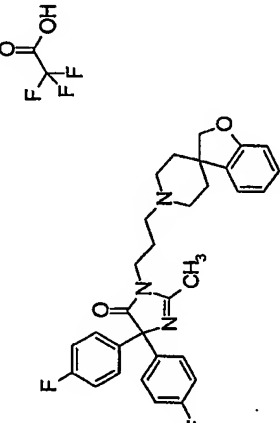
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
303		3-{3-[6-fluoro-spiro(3,4-dihydro-2H-1-benzopyran-4-oxo-2,3'-piperidin)-1'-yl]propyl]-5,5-di(4-fluorophenyl)-2-methyl-1,3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 27 & 30	562.00	2.41	0.25 (DCM:MeOH: TFA=90:9:1)
304		3-{3-[spiro(2,3-dihydrobenzofuran-3,4'-piperidin)-1'-yl]propyl]-5,5-di(4-fluorophenyl)-2-methyl-1,3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 25 & 30	516.00	2.37	0.29 (DCM:MeOH: TFA=90:9:1)

Table 1

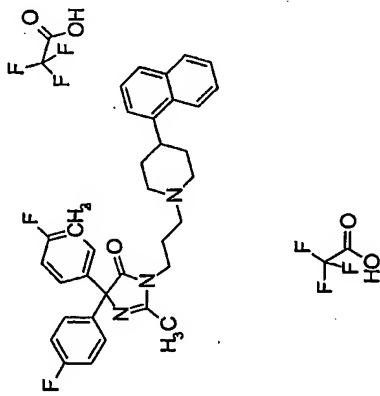
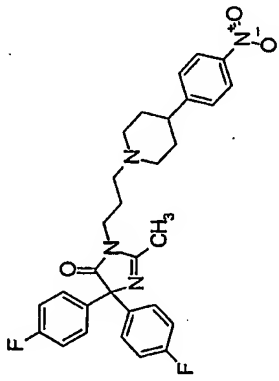
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
305		5,5-di-(4-fluorophenyl)-2-methyl-3-{3-[4-(1-naphthyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one bis(trifluoroacetate)	Example 30	538.00	2.54	RF 0.27 (DCM:MeOH: TFA=90:9:1)
306		5,5-Bis-(4-fluoro-phenyl)-2-methyl-3-{3-[4-(4-nitro-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 28 & 30	533.00	2.41	RF 0.22 (EtOAc:HEX: MeOH=4.5:4.5 :1)

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
307		3-{3-[4-(3-Fluoro-5-nitro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 26 & 30	551.00	2.51	0.23 MeOH:DCM 5:95
308		3-{3-[4-(4-Amino-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	503.00	1.92	0.44 (15%MeOH/ DCM)
309		5,5-Bis-(4-fluoro-phenyl)-3-{2-fluoro-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	573.00	2.52	0.34 MeOH:DCM 5:95

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
310		2-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-N-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide	Example 31	521.00	3.58	0.44 EtOAc:hexane 8:2
311		2-[2-Cyclopropyl-4,4-bis-(4-fluoro-phenyl)-5-oxo-4,5-dihydro-imidazol-1-yl]-N-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide	Example 31	547.00	3.88	0.39 EtOAc:hexane 6:4

Table 1

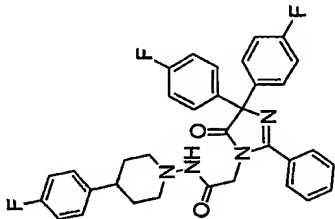
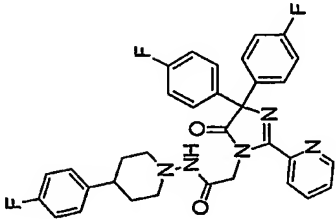
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
312		2-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl]-N-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide	Example 31	583.00	4.02	0.43 EtOAc:hexane 1:1
313		2-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-2-pyridin-2-yl-4,5-dihydro-imidazol-1-yl]-N-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide	Example 31	584.00	3.95	0.31 EtOAc:hexane 1:1

Table 1

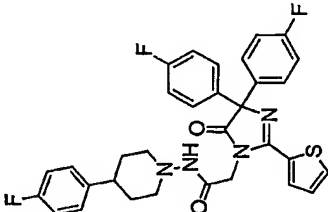
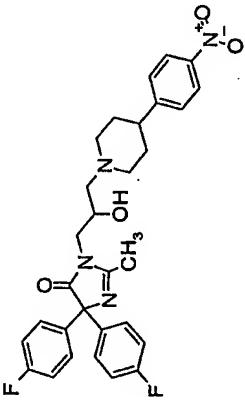
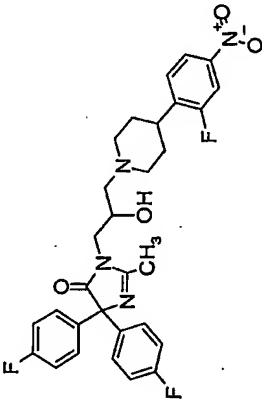
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
314		2-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-2-thiophen-2-yl-4,5-dihydro-imidazol-1-yl]-N-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide	Example 31	589.00	4.10	0.42 EtOAc:hexane 1:1
315		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-[4-(4-nitro-phenyl)-piperidin-1-yl]-propyl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 6	549.00	2.56	0.24 EtOAc:hexane: MeOH 45:45:10
316		3-[3-[4-(2-Fluoro-4-nitro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl]-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 6	567.00	2.48	0.23 EtOAc:hexane: MeOH 45:45:10

Table 1

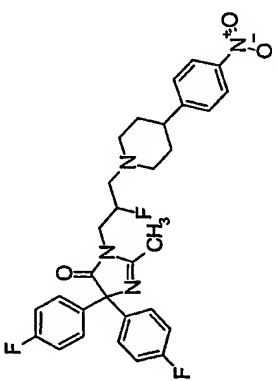
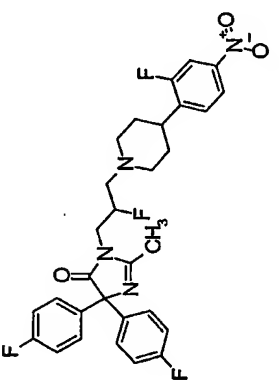
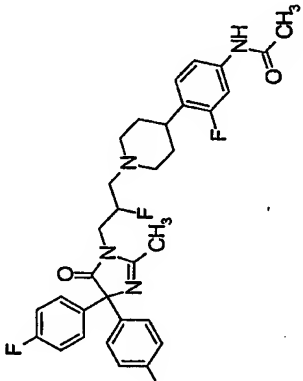
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
317		3-{2-Fluoro-3-[4-(4-nitro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	551.00	2.81	0.59 EtOAc:hexane: MeOH 75:20:5
318		3-{2-Fluoro-3-[4-(2-fluoro-4-nitro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	569.00	2.78	0.58 EtOAc:hexane: MeOH 75:20:5
319		N-[4-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-2-fluoro-propyl}-piperidin-4-yl)-3-fluoro-phenyl]-acetamide	Example 7	581.00	2.42	0.41 EtOAc:hexane: MeOH 45:45:10

Table 1

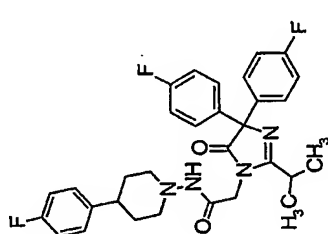
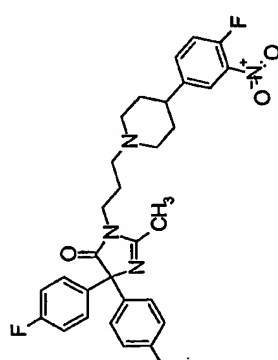
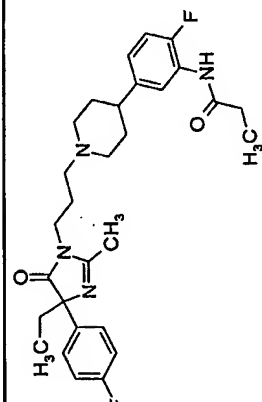
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
320		2-[4,4-Bis-(4-fluoro-phenyl)-2-isopropyl-5-oxo-4,5-dihydro-imidazol-1-yl]-N-[4-(4-fluoro-phenyl)-piperidin-1-yl]-acetamide	Example 31	549.00	3.88	0.36 EtOAc:hexane 1:1
321		3-[3-[4-(4-Fluoro-3-nitro-phenyl)-piperidin-1-yl]-propyl]-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 29 & 30	551.00	2.89	0.14 EtOAc:hexane: MeOH 45:45:10
322		N-[5-(1-[3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-2-fluoro-phenyl]-propionamide	Example 30	511.00	2.56	0.46 EtOAc:hexane: MeOH 40:40:20

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
323		N-[5-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-2-fluoro-phenyl]-isobutyramide	Example 30	525.00	2.52	0.47 EtOAc:hexane: MeOH 40:40:20
324		N-[5-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-2-fluoro-phenyl]-butyramide	Example 30	525.00	2.52	0.47 EtOAc:hexane: MeOH 40:40:20
325		N-[5-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-2-fluoro-phenyl]-propionamide	Example 30	577.00	2.78	0.55 EtOAc:hexane: MeOH 40:40:20

Table 1

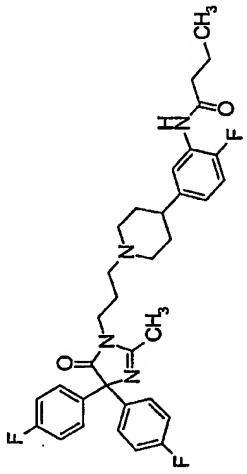
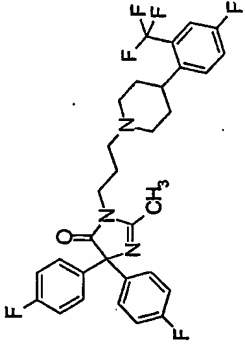
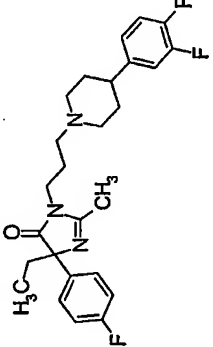
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
326		N-[5-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-2-fluoro-phenyl]-butyramide	Example 30	591.00	2.74	0.59 EtOAc:hexane: MeOH 40:40:20
327		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-11uoro-2-tri1luoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 32 & 30	574.00	2.85	0.56 EtOAc:hexane: MeOH 45:45:10
328		3-{3-[4-(3,4-Difluoro-phenyl)-piperidin-1-yl]-propyl}-5-ethyl-5-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 32 & 30	458.00	2.30	0.45 EtOAc:hexane: MeOH 45:45:10

Table 1

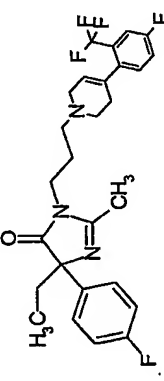
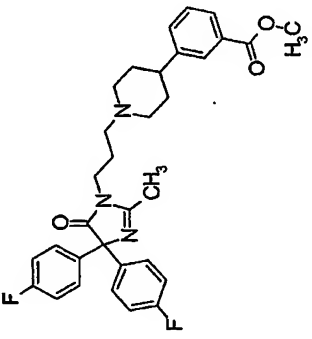
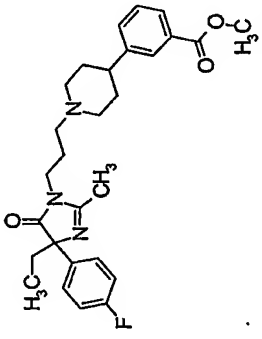
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
329		5-Ethyl-5-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-2-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 32 & 30	506.00	0.25	0.47 EtOAc:hexane: MeOH 45:45:10
330		3-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-benzoic acid methyl ester	Example 30	546.00	2.85	0.35 EtOAc:hexane: MeOH 45:45:10
331		3-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-benzoic acid methyl ester	Example 30	480.00	2.59	0.27 EtOAc:hexane: MeOH 45:45:10

Table 1

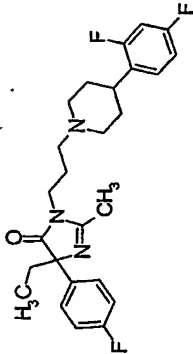
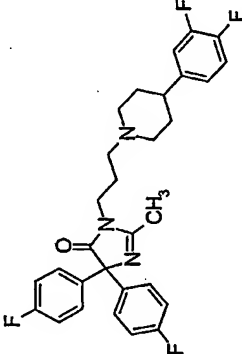
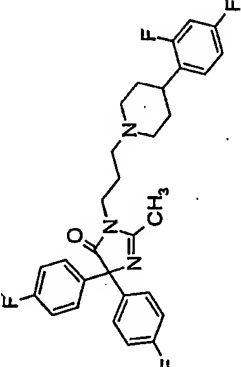
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
332		3-{3-[4-(2,4-Difluoro-phenyl)-piperidin-1-yl]-propyl}-5-ethyl-5-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 33 & 30	458.00	2.29	0.44 EtOAc:hexane: MeOH 45:45:10
333		3-{3-[4-(3,4-Difluoro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-Phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 33 & 30	524.00	2.67	0.55 EtOAc:hexane: MeOH 45:45:10
334		3-{3-[4-(2,4-Difluoro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-Phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 32 & 30	524.00	2.64	0.55 EtOAc:hexane: MeOH 45:45:10

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
335		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-2-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 32 & 30	572.00	3.14	0.55 EtOAc:hexane: MeOH 45:45:10
336		3-[6-trifluoromethyl-spiro(2,3-dihydrobenzofuran-3,4'-piperidin)-1'-yl]propyl-5,5-di(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 25 & 30	584.00	2.56	0.27 EtOAc:hexane: MeOH 45:45:10
337		3-{2-Fluoro-3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	524.00	2.78	0.53 EtOAc:hexane: MeOH 75:20:5

Table 1

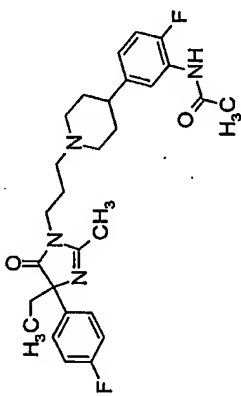
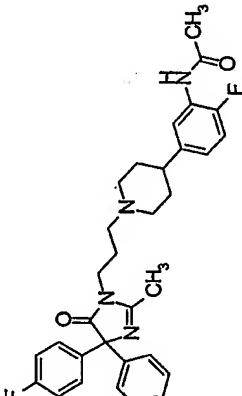
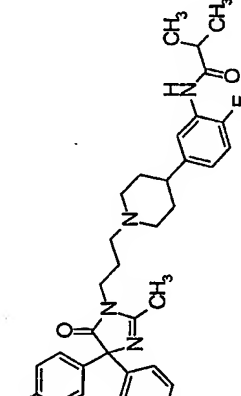
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
338		N-[5-(1-{3-[4-Ethyl-4-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-2-fluoro-phenyl]-acetamide	Example 30	497.00	2.62	0.44 EtOAc:hexane: MeOH 40:40:20
339		N-[5-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-2-fluoro-phenyl]-acetamide	Example 30	563.00	2.63	0.53 EtOAc:hexane: MeOH 40:40:20
340		N-[5-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl]-piperidin-4-yl)-2-fluoro-phenyl]-isobutyramide	Example 30	591.00	2.74	0.57 EtOAc:hexane: MeOH 40:40:20

Table 1

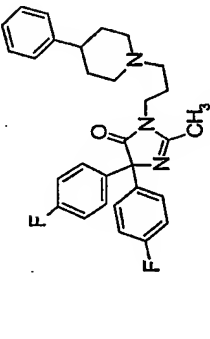
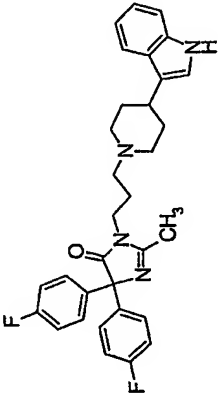
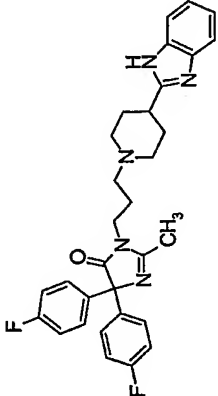
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
341		5,5-Bis-(4-fluoro-phenyl)-2-methyl-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	488.00	2.28	
342		5,5-Bis-(4-fluoro-phenyl)-3-[3-[4-(1H-indol-3-yl)-piperidin-1-yl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	527.00	1.13	
343		3-[3-[4-(1H-Benzimidazol-2-yl)-piperidin-1-yl]-propyl]-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	528.00	2.58	

Table 1

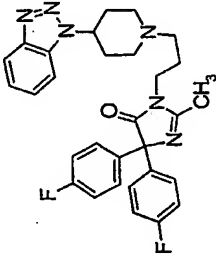
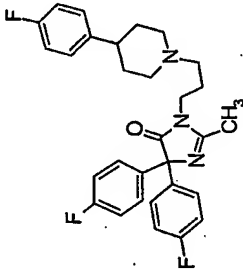
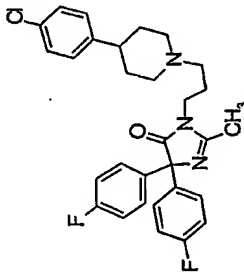
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
344		3-{3-[4-Benzotriazol-1-yl-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	529.00	2.18	
345		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	506.00	2.28	
346		3-{3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	522.00	2.35	

Table 1

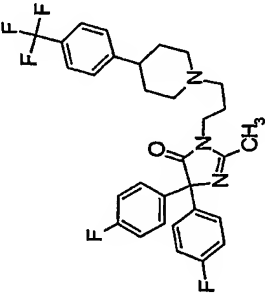
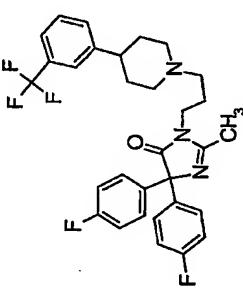
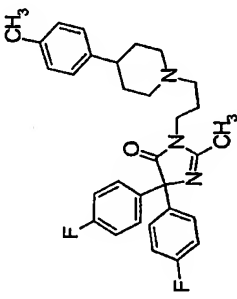
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
347		5,5-Bis-(4-(trifluoromethyl)-2-methyl-3-{3-[4-(4-trifluoromethylphenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	556.00	2.40	
348		5,5-Bis-(4-(trifluoromethyl)-2-methyl-3-{3-[4-(3-trifluoromethylphenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	556.00	2.40	
349		5,5-Bis-(4-(trifluoromethyl)-2-methyl-3-{3-[4-(4-methylphenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	502.00	2.34	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
350		1-(3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl)-4-phenyl-piperidine-4-carbonitrile	Example 30	513.00	2.34	
351		3-{3-[4-(4-Chloro-3-trifluoromethyl-phenyl)-4-hydroxy-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	606.00	2.47	
352		5,5-Bis-(4-fluoro-phenyl)-2-methyl-3-[3-(4-phenyl-piperazin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	489.00	2.50	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
353		5,5-Bis-(4-fluoro-phenyl)-3-(3-[4-(4-fluoro-phenyl)-piperazin-1-yl]-propyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	507.00	2.53	
354		4-(4-{3-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperazin-1-yl)-benzonitrile	Example 30	514.00	2.46	
355		2-Cyclopropyl-5,5-bis-(4-fluoro-phenyl)-3-(3-[4-(4-trifluoromethyl-phenyl)-piperazin-1-yl]-propyl)-3,5-dihydro-imidazol-4-one	Example 30	583.00	2.58	
356		1-(1-{3-[2-Cyclopropyl-4,4-bis-(4-fluoro-phenyl)-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-1,3-dihydro-benzimidazol-2-one	Example 30	570.00	2.21	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
357		8-{3-[2-Cyclopropyl-4,4-bis-(4-fluoro-phenyl)-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-one	Example 30	584.00	2.25	
358		2-Cyclopropyl-5,5-bis-(4-fluoro-phenyl)-3-[3-(4-phenyl-piperazin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	515.00	2.30	
359		2-Cyclopropyl-5,5-bis-(4-(1-fluoro-phenyl)-3,5-dihydro-imidazol-4-one	Example 30	533.00	2.34	

Table 1

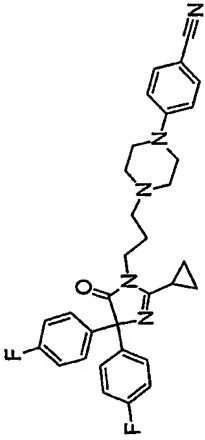
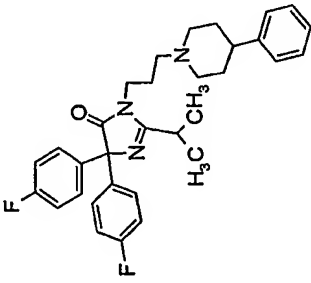
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
360		4-(4-{3-[2-Cyclopropyl-4,4-bis-(4-(1-fluoro-phenyl)-5-oxo-4,5-dihydro-imidazol-1-yl)-propyl]-piperazin-1-yl}-benzonitrile)phenyl	Example 30	540.00	2.36	
361		5,5-Bis-(4-fluoro-phenyl)-2-isopropyl-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-3,5-dihydroimidazol-4-one	Example 30	516.00	2.73	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
362		5,5-Bis-(4-(11-fluoro-phenyl))-2-isopropyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperazin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	585.00	2.89	
363		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 30	534.00	2.76	

Table 1

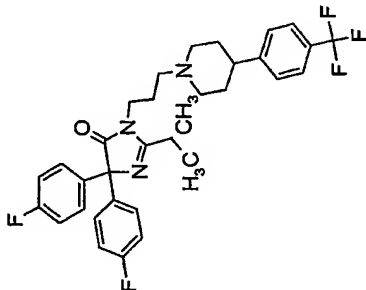
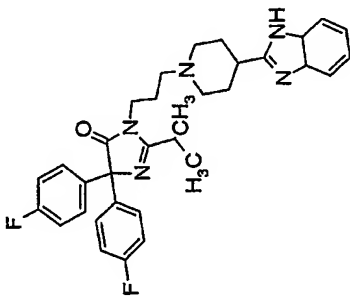
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
364		5,5-Bis-(4-fluoro-phenyl)-2-isopropyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	584.00	2.90	
365		3-{3-[4-(3a,7a-Dihydro-1H-benzoimidazol-2-yl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 30	556.00	2.41	

Table 1

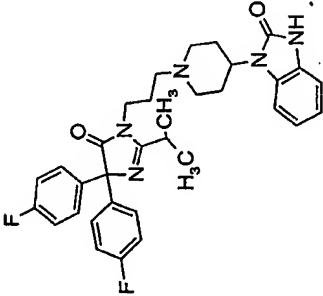
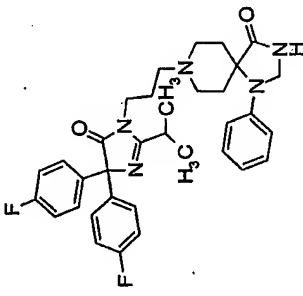
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
366		1-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-2-isopropyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-1,3-dihydro-benzimidazol-2-one	Example 30	572.00	2.54	
367		8-{3-[4,4-Bis-(4-fluoro-phenyl)-2-isopropyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-one	Example 30	586.00	2.64	

Table 1

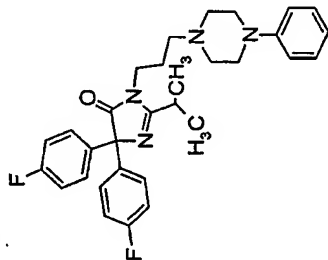
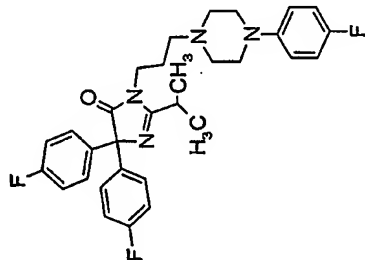
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
368		5,5-Bis-(4-fluoro-phenyl)-2-isopropyl-3-[3-(4-phenyl-piperazin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	517.00	2.67	
369		5,5-Bis-(4-fluoro-phenyl)-3-[3-(4-(4-fluoro-phenyl)-piperazin-1-yl)-propyl]-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 30	535.00	2.78	

Table 1

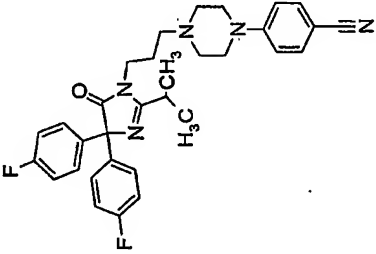
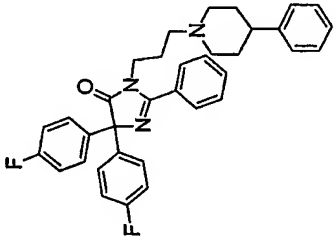
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
370		4-(4-{3-[4,4-Bis-(4-fluoro-phenyl)-2-isopropyl-5-oxo-4,5-dihydro-imidazol-1-yl]-propyl}-piperazin-1-yl)-benzonitrile	Example 30	542.00	2.65	
371		5,5-Bis-(4-fluoro-phenyl)-2-phenyl-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	550.00	2.81	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
372		5,5-Bis-(4-fluoro-phenyl)-2-phenyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperazin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	619.00	2.95	
373		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 30	568.00	2.81	

Table 1

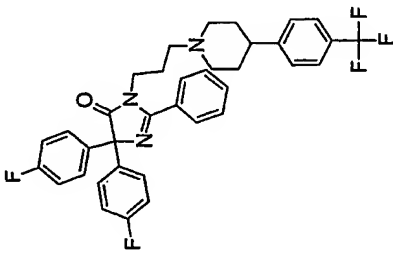
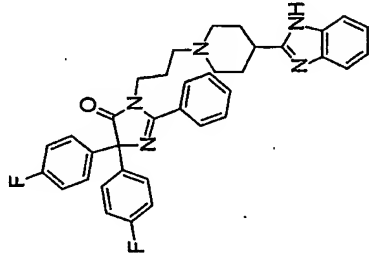
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
374		5,5-Bis-(4-fluoro-phenyl)-2-phenyl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	618.00	3.00	
375		3-{3-[4-(1H-Benzimidazol-2-yl)-piperidin-1-yl]-propyl}-5,5-bis-(4-fluoro-phenyl)-2-phenyl-3,5-dihydro-imidazol-4-one	Example 30	590.00	2.37	

Table 1

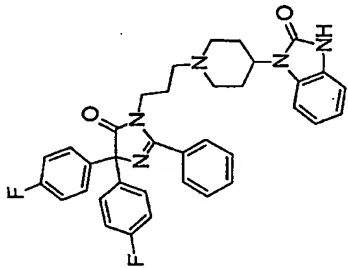
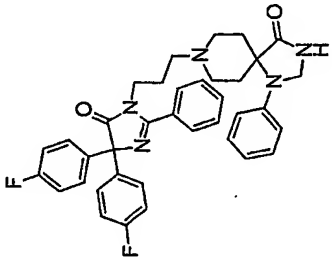
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
376		1-(1-{3-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl]-propyl}-piperidin-4-yl)-1,3-dihydro-benzimidazol-2-one	Example 30	606.00	2.69	
377		8-{3-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl]-propyl}-1-phenyl-1,3,8-triaza-spiro[4.5]decan-4-one	Example 30	620.00	2.80	

Table 1

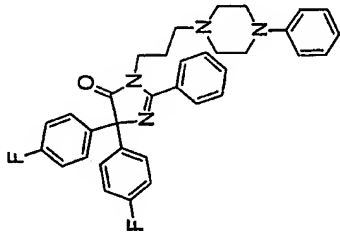
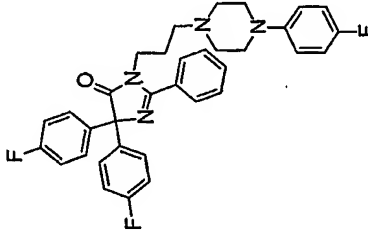
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
378		5,5-Bis-(4-fluoro-phenyl)-2-phenyl-3-[3-(4-phenyl-piperazin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	551.00	2.73	
379		5,5-Bis-(4-fluoro-phenyl)-3-[3-(4-(4-fluoro-phenyl)-piperazin-1-yl)-propyl]-2-phenyl-3,5-dihydro-imidazol-4-one	Example 30	569.00	2.78	

Table 1

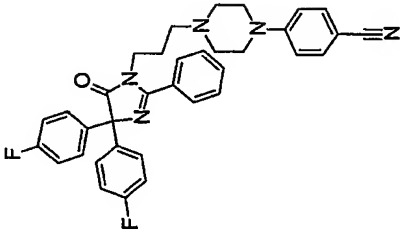
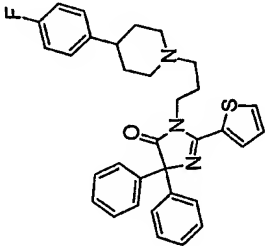
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
380		4-(4-{3-[4,4-Bis-(4-fluoro-phenyl)-5-oxo-2-phenyl-4,5-dihydro-imidazol-1-yl]-propyl}-piperazin-1-yl)-benzonitrile	Example 30	576.00	2.70	
381		3-{3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-propyl}-5,5-diphenyl-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 30	538.00	2.31	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
382		1-[3-(5-oxo-4,4-diphenyl-2-thiophen-2-yl-4,5-dihydro-imidazol-1-yl)-propyl]-4-phenyl-piperidine-4-carbonitrile	Example 30	545.00	2.49	
383		3-{3-[4-(4-chloro-phenyl)-piperidin-1-yl]-propyl}-5,5-diphenyl-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 30	555.00	2.41	
384		5,5-di(phenyl)-2-thiophen-2-yl-3-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	588.00	2.47	

Table 1

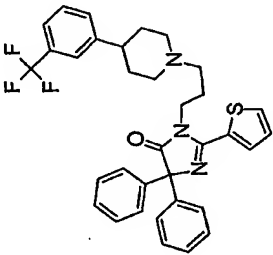
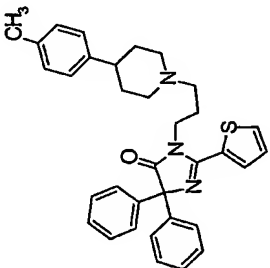
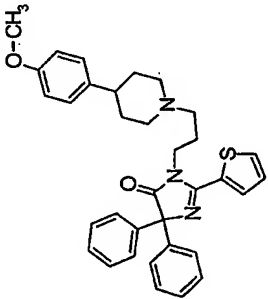
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
385		5,5-Diphenyl-2-thiophen-2-yl-3-{3-[4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 30	588.00	2.46	
386		5,5-Diphenyl-2-thiophen-2-yl-3-[3-(4-p-tolyl-piperidin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	534.00	2.47	
387		3-[3-[4-(4-Methoxy-phenyl)-piperidin-1-yl]-propyl]-5,5-diphenyl-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 30	550.00	2.38	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
388		3-(3-[4-(1H-Indol-3-yl)-piperidin-1-yl]-propyl)-5,5-diphenyl-2-thiophen-2-yl-3,5-dihydroimidazol-4-one	Example 30	560.00	2.33	
389		3-(3-[4-(1H-Benzimidazol-2-yl)-phenyl]-piperidin-1-yl)-propyl)-5,5-diphenyl-2-thiophen-2-yl-3,5-dihydroimidazol-4-one	Example 30	560.00	1.88	
390		3-[2-spiro(25,5-dihydrobenzofuran-2,4'-piperidinyl)propyl]-5,5-di(4-fluorophenyl)-2-(2-thienyl-3,5-dihydro-4H-imidazol-4-one	Example 30	548.00	2.30	

Table 1

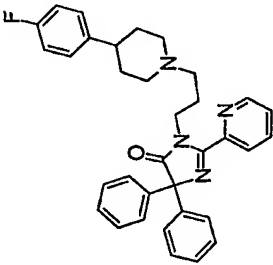
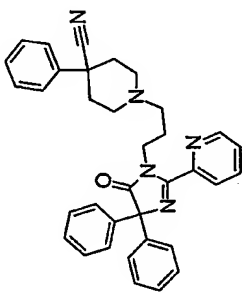
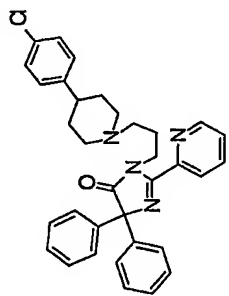
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
391		3-[3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-propyl]-5,5-diphenyl-2-pyridin-2-yl-3,5-dihydro-imidazol-4-one	Example 30	533.00	2.28	
392		1-[3-(5-Oxo-4,4-diphenyl-2-pyridin-2-yl)-4,5-dihydro-imidazol-1-yl]-propyl-4-phenyl-piperidine-4-carbonitrile	Example 30	540.00	2.38	
393		3-[3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-propyl]-5,5-diphenyl-2-pyridin-2-yl-3,5-dihydro-imidazol-4-one	Example 30	549.00	2.37	

Table 1

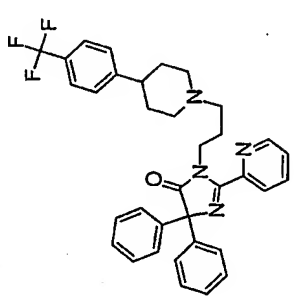
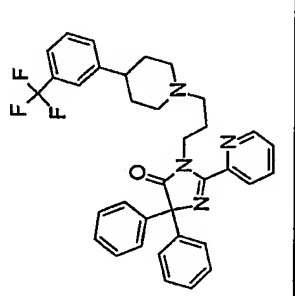
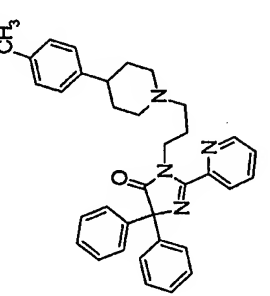
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
394		5,5-Diphenyl-2-pyridin-2-yl-3-[3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl]-3,5-dihydro-imidazol-4-one	Example 30	583.00	2.46	
395		5,5-Diphenyl-2-pyridin-2-yl-3-[3-[4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl]-3,5-dihydro-imidazol-4-one	Example 30	583.00	2.44	
396		5,5-Diphenyl-2-pyridin-2-yl-3-[3-[4-(p-tolyl-piperidin-1-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 30	529.00	2.43	

Table 1

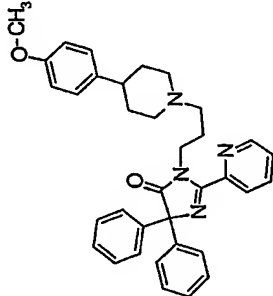
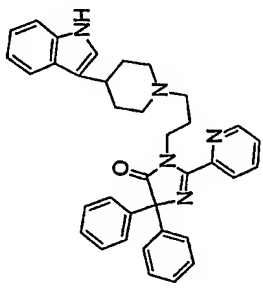
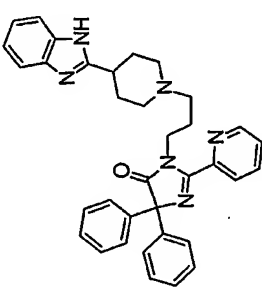
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
397		3-(3-[4-(4-Methoxy-phenyl)-piperidin-1-yl]-propyl)-5,5-diphenyl-2-pyridin-2-yl-3,5-dihydroimidazol-4-one	Example 30	545.00	2.35	
398		3-(3-[4-(1H-Indol-3-yl)-piperidin-1-yl]-propyl)-5,5-diphenyl-2-pyridin-2-yl-3,5-dihydroimidazol-4-one	Example 30	554.00	2.35	
399		3-(3-[4-(1H-Benzimidazol-2-yl)-piperidin-1-yl]-propyl)-5,5-diphenyl-2-pyridin-2-yl-3,5-dihydroimidazol-4-one	Example 30	555.00	2.38	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
400		3-[4-spiro(1-phthalan)piperidin-1-yl]propyl-5,5-diphenyl-2-(2-pyridyl)-3,5-dihydro-4H-imidazol-4-one	Example 30	543.00	2.25	
401		5,5-Bis-(4-fluoro-phenyl)-3-{4-[4-(4-fluoro-phenyl)-piperazin-1-yl]-1-methyl-pentyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	549.00	2.27	

Table 1

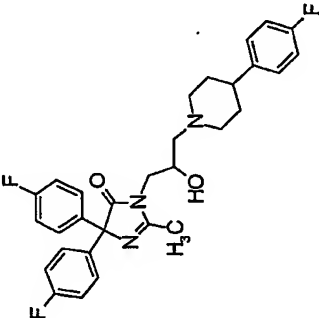
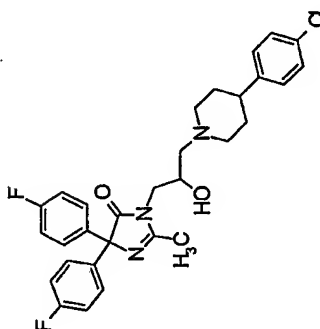
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
402		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 6	522.00	2.26	
403		3-{3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-1luoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 6	539.00	2.34	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
404		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperazin-1-yl]-2-hydroxy-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 6	523.00	2.21	
405		3-[4-spiro(1-phthalan)piperidin]-1-yl-2-hydroxypropyl-5,5-di(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 6	532.00	2.21	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
406		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-methoxy-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 30	518.00	2.26	
407		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-phenyl-piperidin-1-yl)-propyl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	504.00	2.17	0.52 MeOH:DCM 1:9
408		5,5-Bis-(4-(1-fluoro-phenyl))-3-{2-hydroxy-3-[4-(4-methoxy-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	534.00	2.33	0.53 MeOH:DCM 1:10

Table 1

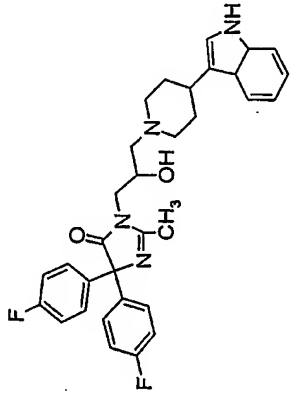
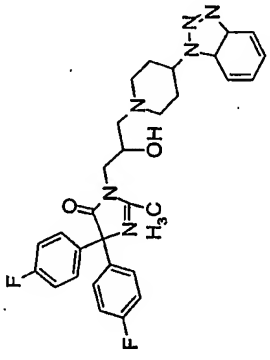
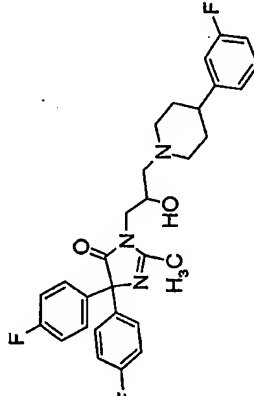
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
409		3-{3-[4-(3a,7a-Dihydro-1H-indol-3-yl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluorophenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	534.00	2.34	0.49 MeOH:DCM 1:10
410		3-{3-[4-(3a,7a-Dihydro-benzotriazol-1-yl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluorophenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	545.00	2.09	0.42 MeOH:DCM 1:10
411		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(3-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	522.00	2.27	0.48 MeOH:DCM 1:10

Table 1

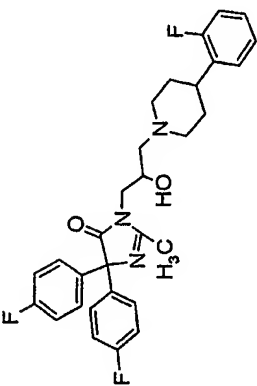
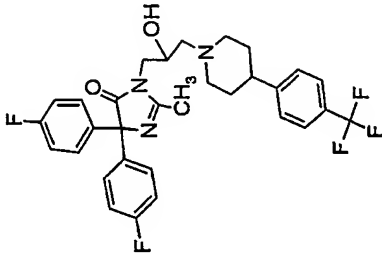
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
412		S,S-Bis-(4-fluoro-phenyl)-S-{S-[4-(2-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-methyl-S,S-dihydro-imidazol-4-one	Example 7	522.00	2.35	0.48 MeOH:DCM 1:10
413		5,5-Bis-(4-11uoro-phenyl)-3-[2-hydroxy-3-[4-(4-tri11uoromethyl-phenyl)-piperidin-1-yl]-propyl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	572.00	2.57	0.22 MeOH:DCM 5:95

Table 1

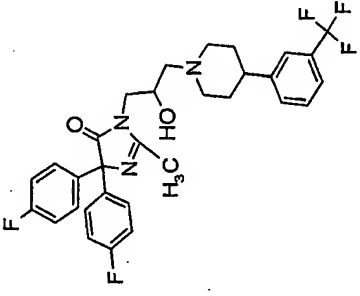
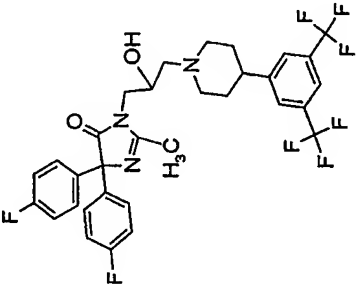
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
414		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	572.00	2.49	0.47 MeOH:DCM 1:9
415		3-{3-[4-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluoro-phenyl)-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	640.00	2.66	0.44 MeOH:DCM 1:9

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
416		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-[3-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl]-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	572.00	2.46	0.65 MeOH:DCM 1:9
417		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-phenyl-piperidin-1-yl)-propyl]-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	566.00	2.44	0.5 MeOH:DCM 1:9
418		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-p-tolyl-piperidin-1-yl)-propyl]-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	580.00	2.53	0.6 MeOH:DCM 1:9

Table 1

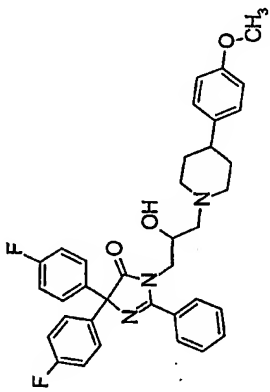
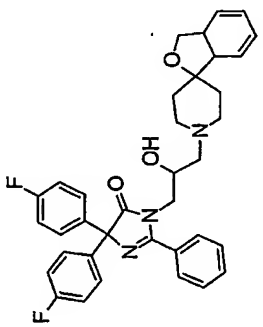
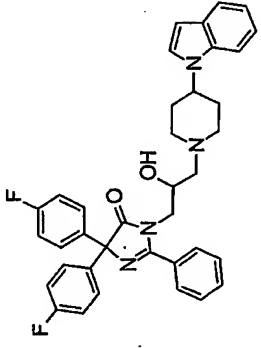
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
419		S,S-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-[4-(4-methoxy-phenyl)-piperidin-1-yl]-propyl]-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	596.00	2.49	0.47 MeOH:DCM 1:9
420		3-[[4-spiro(1-phthalan)piperidin]-1-yl]-2-hydroxypropyl]-5,5-di(4-fluorophenyl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one	Example 7	594.00	2.42	0.49 MeOH:DCM 1:9
421		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-indol-1-yl-piperidin-1-yl)-propyl]-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	605.00	2.58	0.74 MeOH:DCM 1:9

Table 1

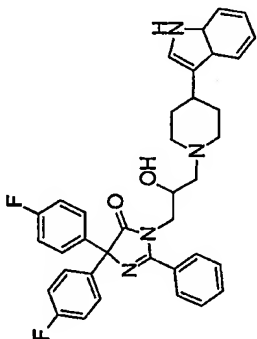
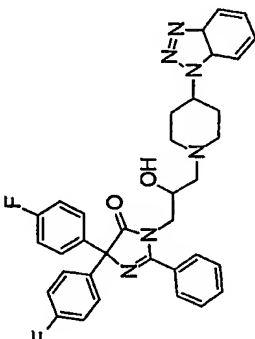
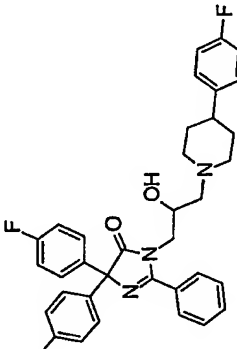
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
422		3-{3-[4-(3a,7a-Dihydro-1H-indol-3-yl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluorophenyl)-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	605.00	2.47	0.30 MeOH:DCM 1:9
423		3-{3-[4-(3a,7a-Dihydro-benzotriazol-1-yl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluorophenyl)-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	607.00	2.33	0.40 MeOH:DCM 1:9
424		5,5-Bis-(4-(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	584.00	2.50	0.50 MeOH:DCM 1:9

Table 1

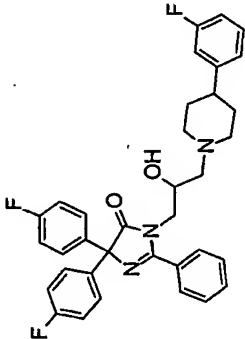
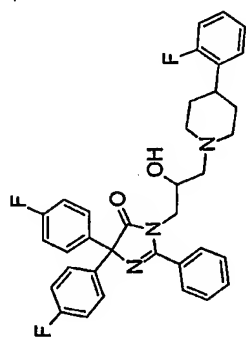
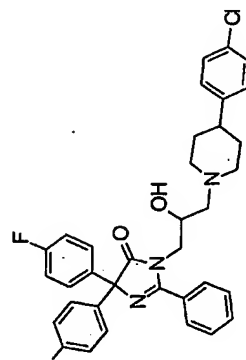
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
425		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(3-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	584.00	2.46	0.58 MeOH:DCM 1:9
426		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(2-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	584.00	2.61	0.56 MeOH:DCM 1:9
427		3-{3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluoro-phenyl)-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	600.00	2.61	0.55 MeOH:DCM 1:9

Table 1

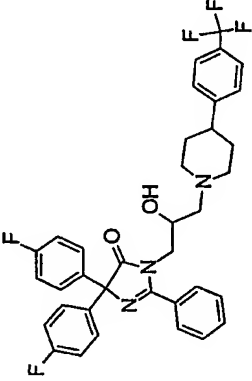
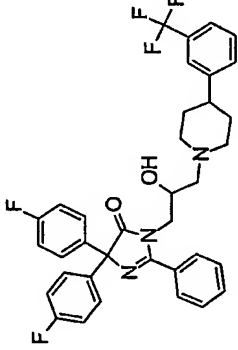
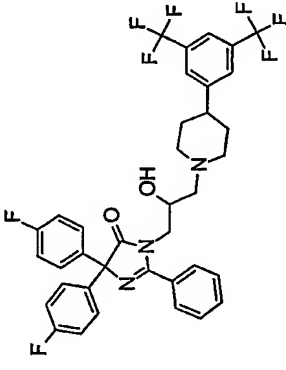
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
428		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	634.00	2.62	0.60 MeOH:DCM 1:9
429		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	634.00	2.64	0.64 MeOH:DCM 1:9
430		3-{3-[4-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluoro-phenyl)-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	702.00	2.77	0.79 MeOH:DCM 1:9

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
431		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[3-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-phenyl-3,5-dihydro-imidazol-4-one	Example 7	634.00	2.69	0.56 MeOH:DCM 1:9
432		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[3-(4-phenyl-piperidin-1-yl)-propyl]-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	532.00	2.47	0.3 MeOH:DCM 5:95

Table 1

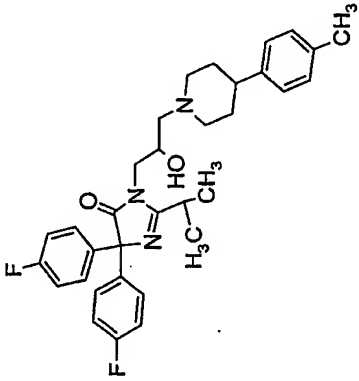
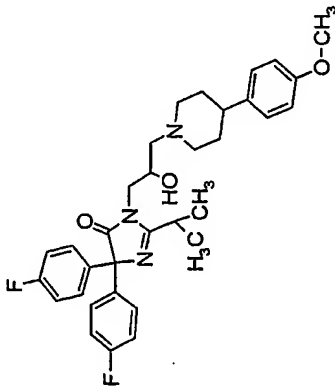
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
433		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-p-tolyl-piperidin-1-yl)-propyl]-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	546.00	2.48	0.2 MeOH:DCM 5:95
434		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-[4-(4-methoxy-phenyl)-piperidin-1-yl]-propyl]-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	562.00	2.41	0.16 MeOH:DCM 5:95

Table 1

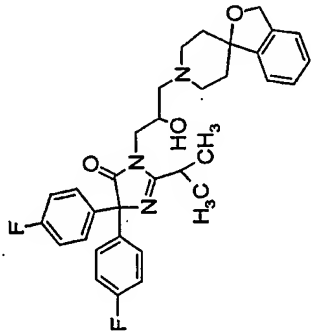
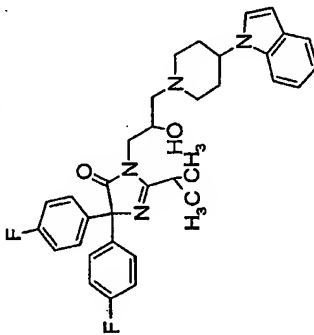
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC. RT (min)	TLC R _f
435		3-[[4-spiro(1-phthalan)piperidin]-1-yl-2-hydroxypropyl]-5,5-di(4-fluorophenyl)-2-isopropyl-3,5-dihydro-4H-imidazol-4-one	Example 7	560.00	2.39	0.16 MeOH:DCM 5:95
436		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-indol-1-yl-piperidin-1-yl)-propyl]-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	571.00	2.53	0.4 MeOH:DCM 5:95

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
437		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(1H-indol-3-yl)-piperidin-1-yl]-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	571.00	2.43	0.07 MeOH:DCM 5:95
438		3-[3-(4-Benzotriazol-1-yl-piperidin-1-yl)-2-hydroxy-propyl]-5,5-bis-(4-fluoro-phenyl)-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	573.00	2.27	0.12 MeOH:DCM 5:95

Table 1

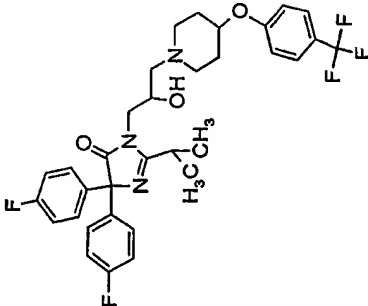
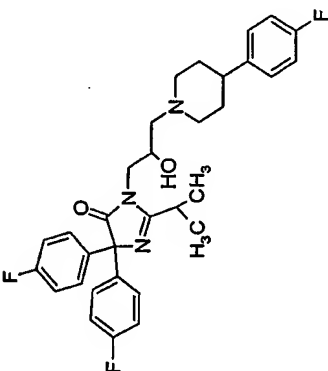
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
439		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-trifluoromethyl-phenoxy)-piperidin-1-yl]-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	616.00	2.64	0.19 MeOH:DCM 5:95
440		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	550.00	2.42	0.26 MeOH:DCM 5:95

Table 1

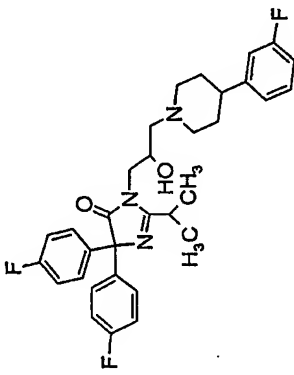
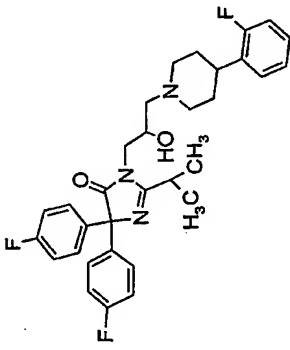
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
441		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(3-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	550.00	2.47	0.26 MeOH:DCM 5:95
442		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(2-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	550.00	2.44	0.28 MeOH:DCM 5:95

Table 1

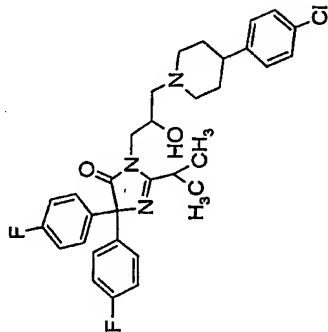
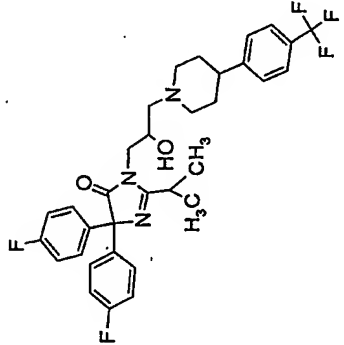
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
443		3-(3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl)-5,5-bis-(4-fluoro-phenyl)-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	566.00	2.56	0.27 MeOH:DCM 5:95
444		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	600.00	2.60	0.22 MeOH:DCM 5:95

Table 1

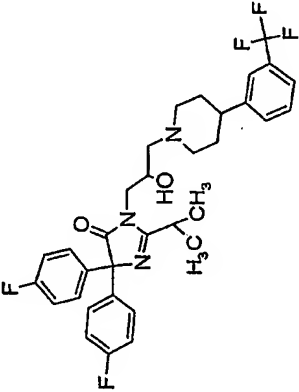
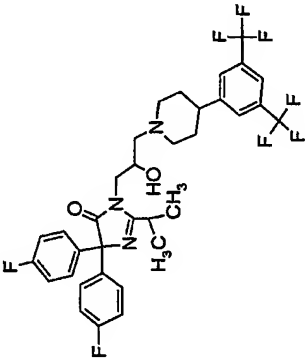
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
445		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	600.00	2.63	0.22 MeOH:DCM 5:95
446		3-{3-[4-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-5,5-bis-(4-fluoro-phenyl)-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	668.00	2.73	0.27 MeOH:DCM 5:95

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
447		5,5-Bis-(4-(11uoro-phenyl))-3-{2-hydroxy-3-[3-(4-tri11uoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-isopropyl-3,5-dihydro-imidazol-4-one	Example 7	600.00	2.66	0.31 MeOH:DCM 5:95
448		5,5-Bis-(4-(4-fluoro-phenyl))-3-[2-hydroxy-3-(4-phenyl-piperidin-1-yl)-propyl]-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	572.00	2.77	0.25 EtOAc:hexane 1:1
449		3-{[4-spiro(1-phthalan)piperidin]-1-yl-2-hydroxypropyl}-5,5-di(4-fluorophenyl)-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one	Example 7	602.00	2.60	0.11 EtOAc:hexane 1:1

Table 1

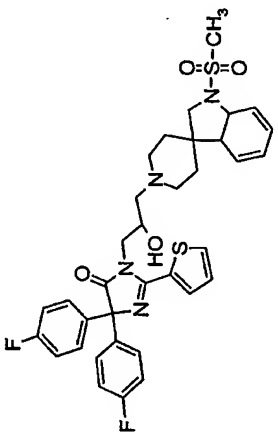
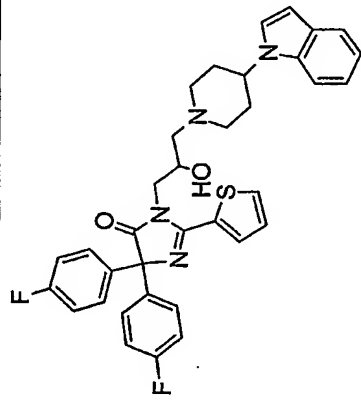
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
450		3-[1-methanesulfonyl-spiro(2,3-indole-3,4'-piperidin)]-1'-yl-2-hydroxypropyl-5,5-di(4-fluorophenyl)-2-(2-thienyl)-3,5-dihydro-4H-imidazol-4-one	Example 7	677.00	2.56	0.10 EtOAc:hexane 1:1
451		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-(4-indol-1-yl-piperidin-1-yl)-propyl]-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	612.00	2.94	0.10 EtOAc:hexane 1:1

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
452		3-[3-(4-Benzotriazol-1-yl)piperidin-1-yl]-2-hydroxypropyl]-5,5-bis-(4-fluoro-phenyl)-2-thiophen-2-yl-3,5-dihydroimidazol-4-one	Example 7	612.00	2.50	0.10 EtOAc:hexane 1:1
453		5,5-Bis-(4-fluoro-phenyl)-3-[2-hydroxy-3-[4-(4-trifluoromethylphenoxy)piperidin-1-yl]propyl]-2-thiophen-2-yl-3,5-dihydroimidazol-4-one	Example 7	656.00	2.84	0.20 EtOAc:hexane 1:1
454		5,5-Bis-(4-fluoro-phenyl)-3-[3-[4-(4-fluoro-phenyl)piperidin-1-yl]-2-hydroxypropyl]-2-thiophen-2-yl-3,5-dihydroimidazol-4-one	Example 7	590.00	2.62	0.19 EtOAc:hexane 1:1

Table 1

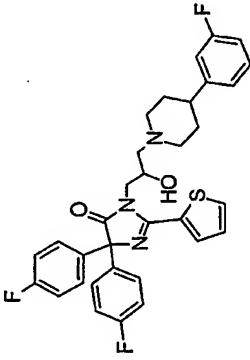
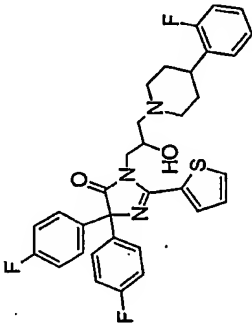
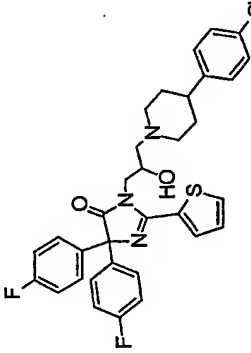
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
455		5,5-Bis-(4-fluoro-phenyl)-3-[3-[4-(3-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl]-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	590.00	2.77	0.22 EtOAc:hexane 1:1
456		5,5-Bis-(4-fluoro-phenyl)-3-[3-[4-(2-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl]-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	590.00	2.70	0.29 EtOAc:hexane 1:1
457		3-[3-[4-(4-Chloro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl]-5,5-bis-(4-fluoro-phenyl)-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	606.00	2.89	0.18 EtOAc:hexane 1:1

Table 1

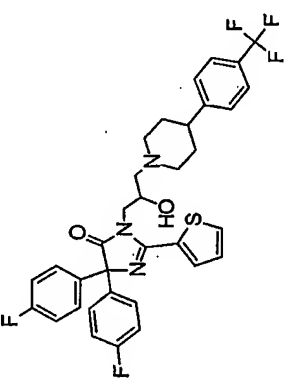
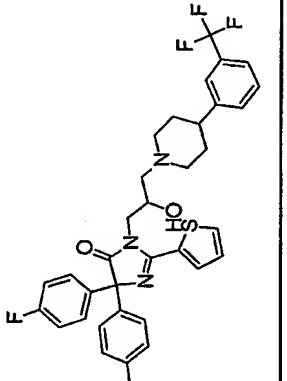
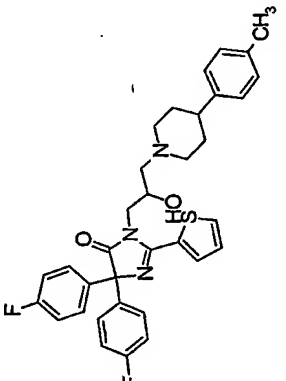
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
458		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	640.00	2.77	0.22 EtOAc:hexane 1:1
459		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(3-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	640.00	2.77	0.26 EtOAc:hexane 1:1
460		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-p-tolyl-piperidin-1-yl)-propyl]-2-thiophen-2-yl}-3,5-dihydro-imidazol-4-one	Example 7	586.00	2.84	0.2 EtOAc:hexane 1:1

Table 1

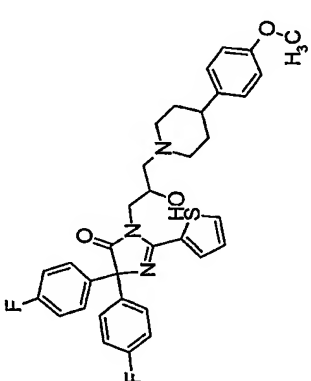
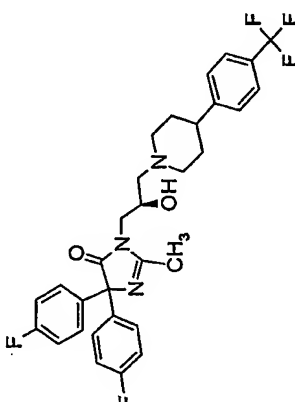
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
461		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-methoxy-phenyl)-piperidin-1-yl]-propyl}-2-thiophen-2-yl-3,5-dihydro-imidazol-4-one	Example 7	602.00	2.60	0.14 EtOAc:hexane 1:1
462		5,5-Bis-(4-(1-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-(trifluoromethyl)-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	572.00	2.62	0.35 MeOH:DCM 5:95

Table 1

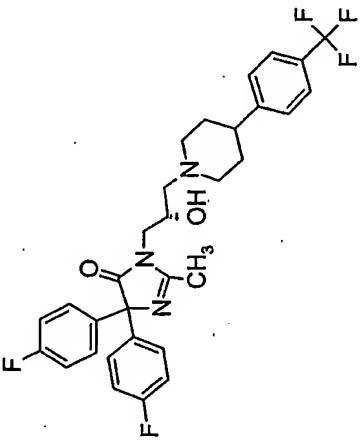
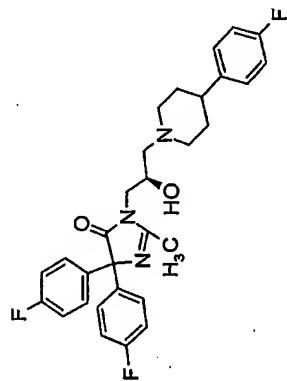
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
463		5,5-Bis-(4-fluoro-phenyl)-3-{2-hydroxy-3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	572.00	2.54	0.35 MeOH:DCM 5:95
464		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	522.00	2.46	0.43 MeOH:DCM 1:9

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
465		5,5-Bis-(4-fluoro-phenyl)-3-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-2-hydroxy-propyl}-2-methyl-3,5-dihydro-imidazol-4-one	Example 7	522.00	2.51	0.43 MeOH:DCM 1:9
466		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-spiro[indane-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	514.00	2.26	0.3 MeOH:DCM 5:95

Table 1

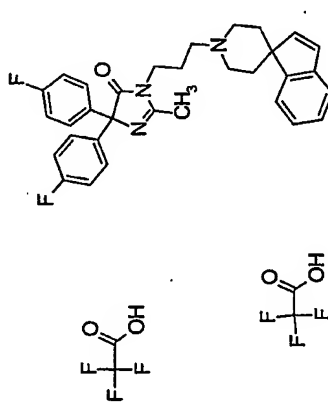
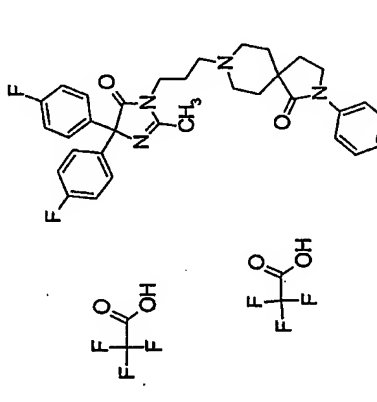
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
467		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-spiro[indene-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	512.00	2.37	0.32 MeOH:DCM 5:95
468		2,8-diaza-8-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolyl)]propyl}-2-methyl-5-oxo(2-imidazolyl)]propyl}-2-phenylspiro[4.5]decan-1-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	557.00	2.19	0.25 MeOH:DCM 5:95

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
469		4,4-bis(4-fluorophenyl)-1-(2-hydroxy-3-spiro[indane-1,4'-piperidine]-10-ylpropyl)-2-methyl-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 6	530.00	2.34	0.46 MeOH:DCM 5:95
470		4,4-bis(4-fluorophenyl)-1-(2-hydroxy-3-spiro[indane-1,4'-piperidine]-10-ylpropyl)-2-methyl-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 6	528.00	2.34	0.46 MeOH:DCM 5:95

Table 1

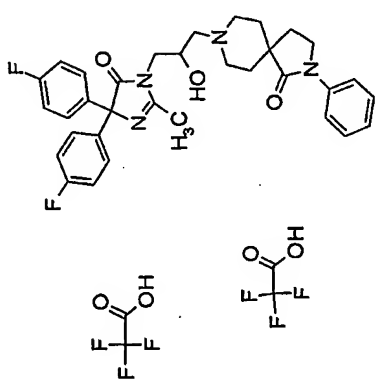
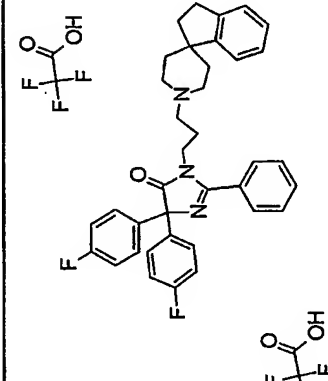
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
471		8-{3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazo[1-y]-2-hydroxypropyl]-2-phenyl-2,8-diazaspiro[4.5]decan-1-one bis(trifluoroacetate)}	Example 6	573.00	2.23	0.42 MeOH:DCM 5:95
472		4,4-bis(4-fluorophenyl)-2-phenyl-1-(3-spiroindane-1,4'-piperidine)-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetate	Example 30	576.00	2.63	0.46 MeOH:DCM 5:95

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
473		4,4-bis(4-fluorophenyl)-2-phenyl-1-(3-spiro[indene-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	574.00	2.63	0.50 MeOH:DCM 5:95
474		8-[3-[4,4-bis(4-fluorophenyl)-5-oxo-2-phenyl-4,5-dihydro-1H-imidazol-1-yl]propyl]-2-phenyl-2,8-diazaspiro[4.5]decan-1-one bis(trifluoroacetate)	Example 30	619.00	2.52	0.39 MeOH:DCM 5:95
475		5,5-Bis-(4-fluoro-phenyl)-3-{2-[4-(4-fluoro-phenyl)-piperidin-1-yl]-ethyl}-2-methyl-3,5-dihydro-imidazol-4-one; compound with trifluoroacetic acid	Example 30	492.00	2.39	0.29 MeOH:DCM 5:95

Table 1

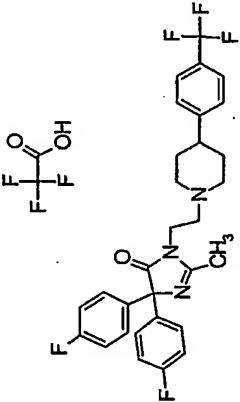
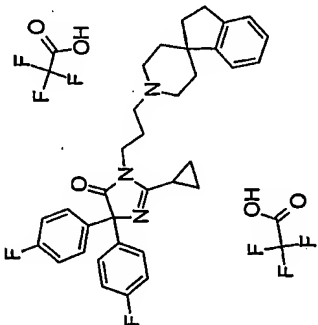
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
476		5,5-Bis-(4-fluoro-phenyl)-2-methyl-3-{2-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-ethyl}-3,5-dihydro-imidazol-4-one; compound with trifluoroacetic acid	Example 30	542.00	2.50	0.32 MeOH:DCM 5:95
477		3-{3-[spiro(indane-1,4'-piperidin)-1'-yl]propyl}-5,5-bis(4-fluorophenyl)-2-cyclopropyl-3,5-dihydro-imidazol-4-one bis(trifluoroacetate)	Example 30	540.00	2.63	0.34 MeOH:DCM 5:95

Table 1

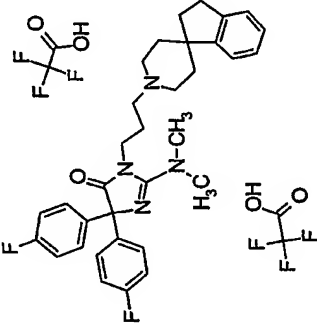
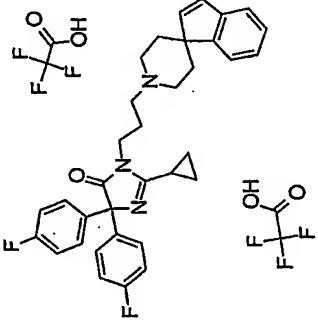
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
478		4,4-bis(4-fluorophenyl)-2-(dimethylamino)-1-(3-spiro[indane-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	543.00	2.12	0.37 MeOH:DCM 5:95
479		4,4-bis(4-fluorophenyl)-2-cyclopropyl-1-(3-spiro[indene-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	538.00	2.56	0.40 MeOH:DCM 5:95

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
480		4,4-bis(4-fluorophenyl)-2-(dimethylamino)-1-(3-spiro[indene-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 30	541.00	2.26	0.41 MeOH:DCM 5:95
481		8-[3-[2-(dimethylamino)-4,4-bis(4-fluorophenyl)-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl]-2-phenyl-2,8-diazaspiro[4.5]decan-1-one bis(trifluoroacetate)	Example 30	586.00	2.19	0.35 MeOH:DCM 5:95

Table 1

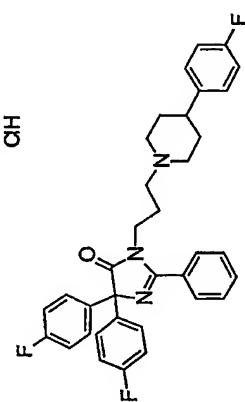
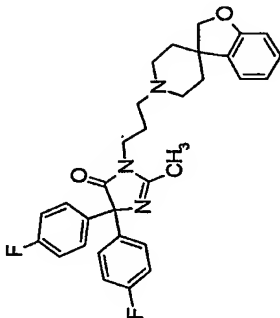
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
482	 <p>OH</p>	5,5-Bis(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)]-1-piperidinyl}propyl-2-phenyl-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 30	568.00	2.90	0.54 MeOH:DCM 5:95
483		5,5-bis(4-fluorophenyl)-2-methyl-3-[3-(1H-spiro[1-benzofuran-3,4'-piperidin]-1'-yl)propyl]-3,5-dihydro-4H-imidazol-4-one	Example 30	516.00	3.19	0.16 MeOH:DCM 5:95

Table 1

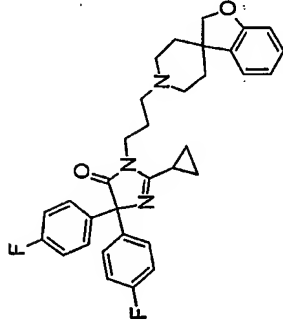
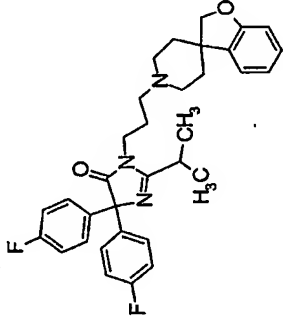
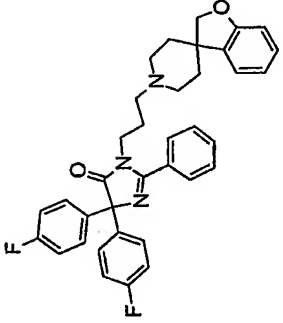
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
484		4,4-bis(4-fluorophenyl)-2-cyclopropyl-1-(3-ylpropyl)-2-imidazolin-5-one	Example 30	542.00	3.34	0.18 MeOH:DCM 5:95
485		4,4-bis(4-fluorophenyl)-2-(methylethyl)-1-(3-ylpropyl)-2-imidazolin-5-one	Example 30	544.00	3.37	0.23 MeOH:DCM 5:95
486		4,4-bis(4-fluorophenyl)-2-phenyl-1-(3-ylpropyl)-2-imidazolin-5-one	Example 30	578.00	2.79	0.3 MeOH:DCM 5:95

Table 1

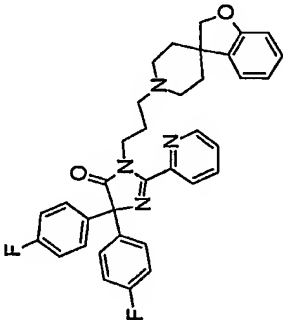
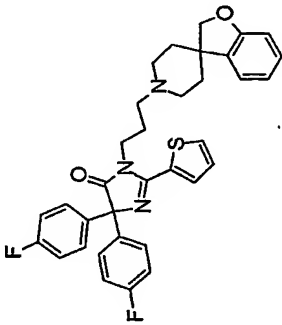
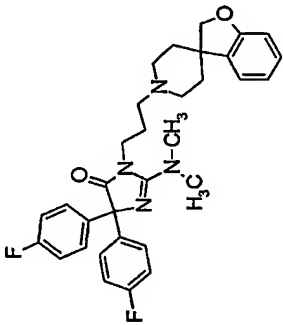
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
487		4,4-bis(4-fluorophenyl)-2-(2-pyridyl)-1-(3-spiro[2,3-dihydrobenzo[b]furan-3,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one	Example 30	579.00	3.45	0.37 MeOH:DCM 5:95
488		4,4-bis(4-fluorophenyl)-1-(3-spiro[2,3-dihydrobenzo[b]furan-3,4'-piperidine]-10-ylpropyl)-2-(2-thienyl)-2-imidazolin-5-one	Example 30	584.00	3.49	0.37 MeOH:DCM 5:95
489		4,4-bis(4-fluorophenyl)-2-(dimethylamino)-1-(3-spiro[2,3-dihydrobenzo[b]furan-3,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one	Example 30	545.00	2.15	0.13 MeOH:DCM 5:95

Table 1

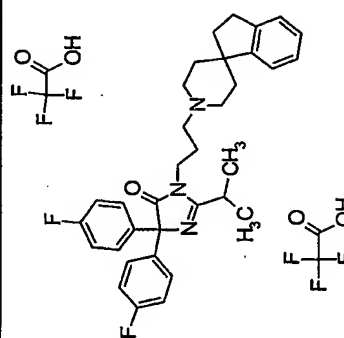
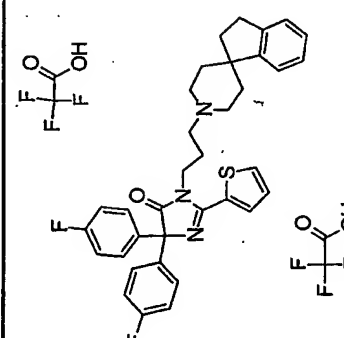
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
490		4,4-bis(4-fluorophenyl)-2-(methylethyl)-1-(3-spiro[indane-1,4'-piperidine]-10-yloxy)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	542.00	2.67	0.53 (DCM:MEOH: TFA 90:9:1)
491		4,4-bis(4-fluorophenyl)-1-(3-spiro[indane-1,4'-piperidine]-10-yloxy)-2-(2-thienyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid, 2,2,2-trifluoroacetic acid	Example 30	582.00	2.78	0.36 (DCM:MEOH: TFA 90:9:1)

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
492		4,4-bis(4-fluorophenyl)-2-(methylethyl)-1-(3-spiro[indene-1,4'-piperidine]-10-ylpropyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 30	540.00	2.74	0.63 (DCM:MeOH: TFA 90:9:1)
493		4,4-bis(4-fluorophenyl)-1-(3-spiro[indene-1,4'-piperidine]-10-ylpropyl)-2-(2-thienyl)-2-imidazolin-5-one, 2,2,2-trifluoroacetic acid	Example 30	580.00	2.84	0.36 (DCM:MeOH: TFA 90:9:1)

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
494		8-{3-[4,4-bis(4-fluorophenyl)-2-isopropyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-2-phenyl-2,8-diazaspiro[4.5]decan-1-one bis(trifluoroacetate)	Example 30	585.00	2.59	0.43 (DCM:MeOH: TFA 90:9:1)
495		8-{3-[4,4-bis(4-fluorophenyl)-5-oxo-2-(2-thienyl)-4,5-dihydro-1H-imidazol-1-yl]propyl}-2-phenyl-2,8-diazaspiro[4.5]decan-1-one bis(trifluoroacetate)	Example 30	625.00	2.70	0.27 (DCM:MeOH: TFA 90:9:1)
496		3-{3-[4-(3-aminophenyl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 9	437.47	2.59	0.35 CH ₃ OH:EtOAc 6:4

Table 1

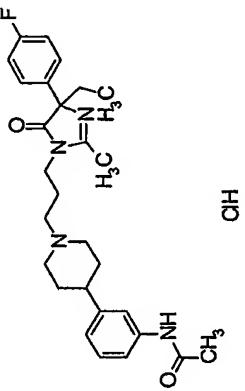
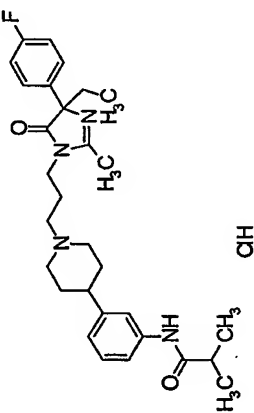
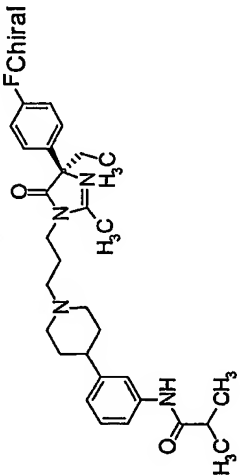
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
497		N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide hydrochloride	Example 30	479.50	2.41	0.33 CH ₃ OH:EtOAc 6:4
498		N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide hydrochloride	Example 30	507.54	2.81	0.41 CH ₃ OH:EtOAc 6:4
499		N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide	Example 30	507.54	2.37	0.41 CH ₃ OH:EtOAc 6:4

Table 1

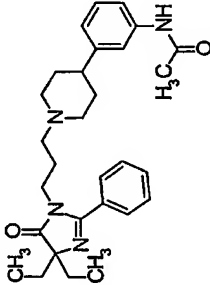
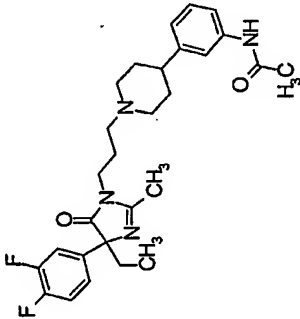
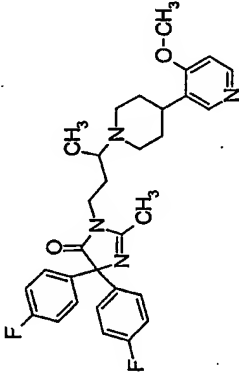
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
500		N-(3-{1-[3-(4,4-diethyl-5-oxo-2-phenyl-4,5-dihydro-1H-imidazol-1-yl)propyl]-4-piperidinyl}phenyl)acetamide	Example 2 & 16	475.30	1.85	0.37 95%CH ₂ Cl ₂ / 4%MeOH/ 1%NH ₄ OH
501		N-[3-(1-[3-(4-(3,4-difluorophenyl)-4-ethyl-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl)propyl]-4-piperidinyl)phenyl]acetamide	Example 8 & 16	497.40	2.56	0.44 90%CH ₂ Cl ₂ / 10%MeOH
502		5,5-bis(4-fluorophenyl)-3-{3-[4-(4-methoxy-3-pyridinyl)-1-piperidinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 4	533.30	1.91	

Table 1

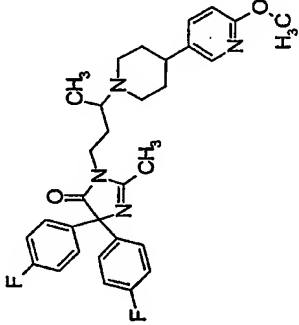
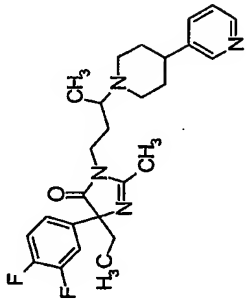
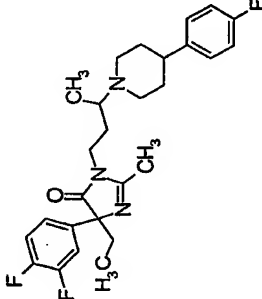
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
503		5,5-bis(4-fluorophenyl)-3-{3-[4-(6-methoxy-3-pyridinyl)-1-piperidinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 4	533.30	2.32	
504		5-(3,4-difluorophenyl)-5-ethyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]butyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	455.30	1.39	
505		5-(3,4-difluorophenyl)-5-ethyl-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]butyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	472.30	2.33	

Table 1

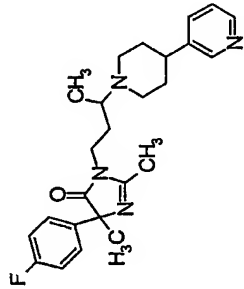
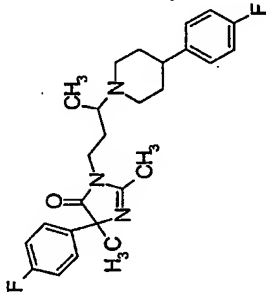
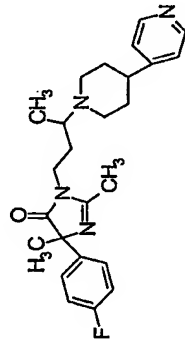
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
506		5-(4-fluorophenyl)-2,5-dimethyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]butyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	423.10	0.75	
507		5-(4-fluorophenyl)-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]butyl}-2,5-dimethyl-1H-imidazol-4-one	Example 2 & 4	440.10	2.21	
508		5-(4-fluorophenyl)-2,5-dimethyl-3-{3-[4-(4-pyridinyl)-1-piperidinyl]butyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	423.20	0.71	

Table 1

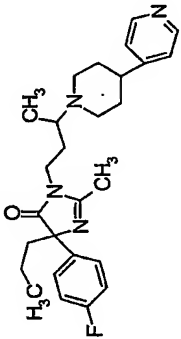
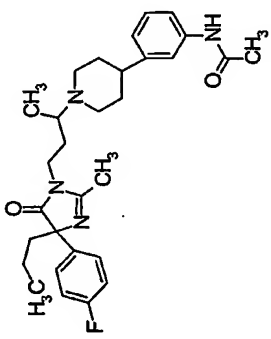
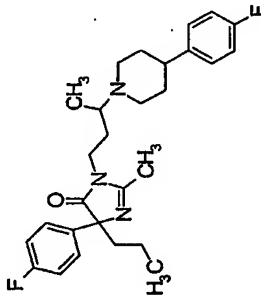
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
509		5-(4-fluorophenyl)-2-methyl-5-propyl-3-(3-[4-(4-pyridinyl)-1-piperidinyl]butyl)-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	451.20	1.48	
510		N-[3-(1-{3-[4-(4-fluorophenyl)-2-methyl-5-oxo-4-propyl-4,5-dihydro-1H-imidazol-1-yl]-1-methylpropyl]-4-piperidinyl)phenyl]acetamide	Example 2 & 4	507.20	2.17	
511		5-(4-fluorophenyl)-3-(3-[4-(4-fluorophenyl)-1-piperidinyl]butyl)-2-methyl-5-propyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	468.20	2.40	

Table 1

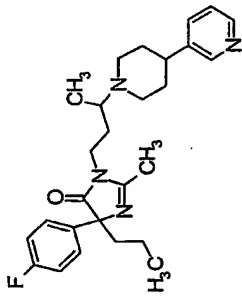
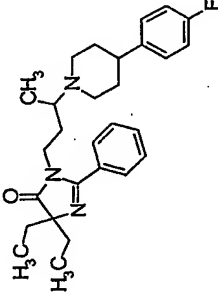
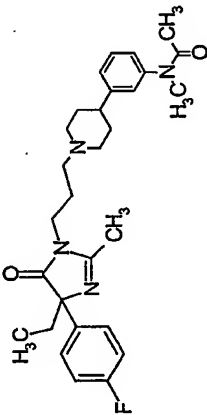
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
512		5-(4-fluorophenyl)-2-methyl-5-propyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]butyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 4	451.10	1.54	
513		5,5-diethyl-3-{3-[4-(4-fluorophenyl)-1-piperidinyl]butyl}-2-phenyl-3,5-dihydro-4H-imidazol-4-one	Example 4	450.20	2.19	
514		N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-N-methylacetamide	Example 8 & 16	493.20	2.00	0.62 4%MeOH/ 1%NH4OH/ 95%CH2CH12

Table 1

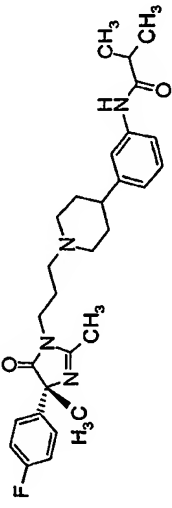
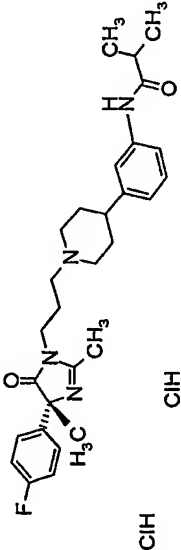
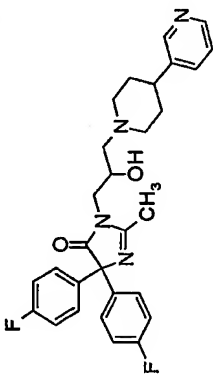
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
515		N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide	Example 5 & 16	493.40	1.97	0.55 4%MeOH/ 1%NH ₄ OH/ 95%CH ₂ Cl ₂
516	 ClH	N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]-2-methylpropanamide dihydrochloride	Example 5 & 16	493.50	1.98	No TLC on salt
517		5,5-bis(4-fluorophenyl)-3-{2-hydroxy-3-[4-(3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 6	505.45	2.34	0.25 (20%MeOH/ 40%EtOAc/ 40%HEXANE)

Table 1

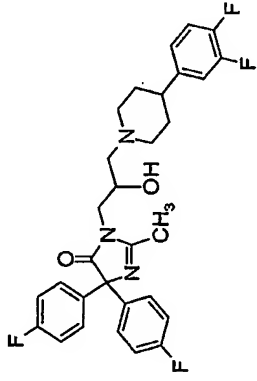
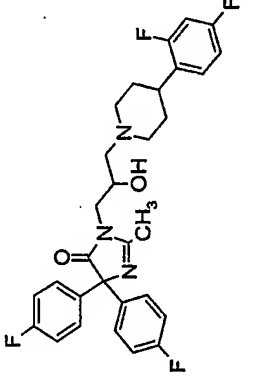
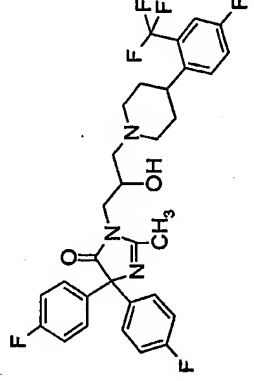
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
518		3-{3-[4-(3,4-difluorophenyl)-1-piperidinyl]-2-hydroxypropyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 6	540.43	3.03	0.34 (20%MEOH/ 40%ETOAC/ 40%HEXANE)
519		3-{3-[4-(2,4-difluorophenyl)-1-piperidinyl]-2-hydroxypropyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 6	540.40	2.70	0.62 (20%MEOH/ 40%ETOAC/ 40%HEXANE)
520		5,5-bis(4-fluorophenyl)-3-{3-[4-[4-fluoro-2-(trifluoromethyl)phenyl]-1-piperidinyl]-2-fluorophenyl}-3-(3-{4-[4-fluoro-2-(trifluoromethyl)phenyl]-1-piperidin	Example 6	590.42	3.03	0.78 (20%MEOH/ 40%ETOAC/ 40%HEXANE)

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
521		methyl 4-(1-(3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl)-4-piperidyl)benzoate	Example 30	480.48	2.78	0.65 (20%MeOH/ 40%EtOAc/ 40%Hexane)
522		5-ethyl-5-(4-fluorophenyl)-3-(3-(4-[4-fluoro-2-(trifluoromethyl)phenyl]-1-piperidyl)propyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 33 & 30	506.43	2.81	0.65 (20%MeOH/ 40%EtOAc/ 40%Hexane)
523		N-[3-(1-(3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl)-4-piperidyl)phenyl]acetamide	Example 34	545.49	2.74	0.20 (20%MeOH/ 40%EtOAc/ 40%Hexane)
524		5-ethyl-3-(3-[4-(4-fluoro-3-nitrophenyl)-1-piperidyl]propyl)-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 26 & 30	485.44	2.96	0.34 (20%MeOH/ 40%EtOAc/ 40%Hexane)

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
525		4-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-N-methylbenzamide	Example 34	479.50	2.37	0.22 (40%ETOAC/ 40%HEXANE/ 20%MEOH)
526		3-{3-[4-(3-aminophenyl)-1-piperidinyl]-2-hydroxypropyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 6	453.48	0.25	0.44 (HEXANE: ETOAC:MEOH: NH4OH = 40:40:18:2)
527		3-{3-[4-(3-aminophenyl)-1-piperidinyl]propyl}-5-(4-fluorophenyl)-2,5-dimethyl-3,5-dihydro-4H-imidazol-4-one	Example 30	423.50	0.32	0.5 (HEXANE: ETOAC:MEOH: NH4CL = 40:40:18:2)
528		(5R)-3-{3-[4-(3-aminophenyl)-1-piperidinyl]propyl}-5-(4-fluorophenyl)-2,5-dimethyl-3,5-dihydro-4H-imidazol-4-one	Example 30	423.49	0.28	0.5 (HEXANE: ETOAC:MEOH: NH4CL = 40:40:18:2)

Table 1

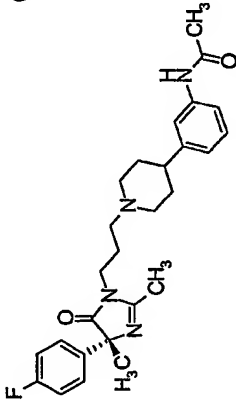
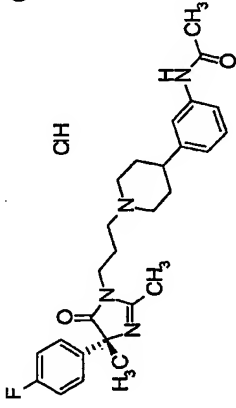
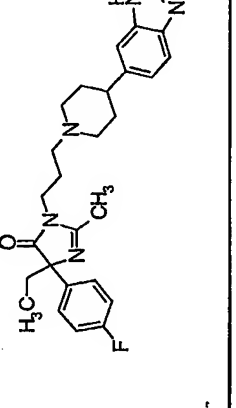
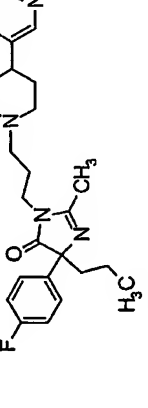
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
529		N-[3-(1-{3-[(4R)-4-(4-fluorophenyl)-2,4-dimethyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide	Example 30	465.49	0.32	0.43 (HEXANE: ETOAC:MEOH :NH ₄ CL = 40:40:18:2)
530		N-[3-(1-{3-[(4R)-4-(4-fluorophenyl)-2,4-dimethyl-5-oxo-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)phenyl]acetamide hydrochloride	Example 30	465.20	1.89	0.2 (DCM:MEOH: TFA = 89:10:1)
531		3-{3-[4-(1H-benzimidazol-6-yl)-1-piperidinyl]propyl}-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 33 & 30	462.49	0.28	0.37 (HEXANE: ETOAC:MEOH :NH ₄ CL = 40:40:18:2)
532		5-(4-fluorophenyl)-2-methyl-5-propyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one	Example 2 & 16	437.30	1.28	

Table 1

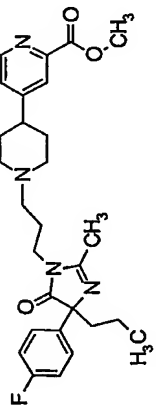
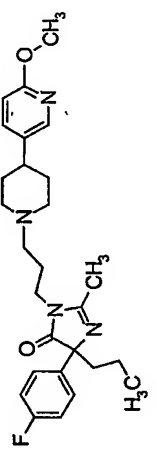
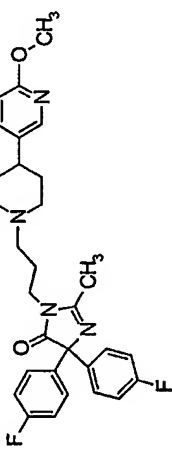
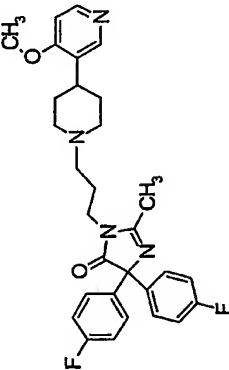
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
533		methyl 4-(1-{3-[4-(4-fluorophenyl)-2-methyl-5-oxo-4-propyl-4,5-dihydro-1H-imidazol-1-yl]propyl}-4-piperidinyl)-2-pyridinecarboxylate	Example 2 & 16	495.40	1.95	
534		5-(4-fluorophenyl)-3-{3-[4-(6-methoxy-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-5-propyl-3,5-dihydro-4H-imidazol-4-one	Example 5, 8, & 16	467.30	2.03	
535		5,5-bis(4-fluorophenyl)-3-{3-[4-(6-methoxy-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 16	519.30	1.85	
536		5,5-bis(4-fluorophenyl)-3-{3-[4-(4-methoxy-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2 & 16	519.40	2.24	

Table 1

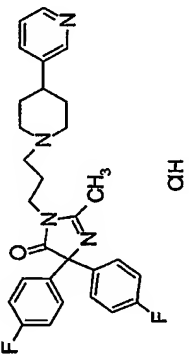
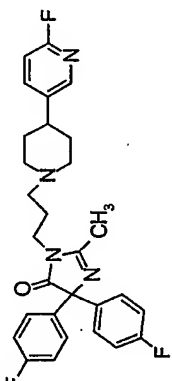
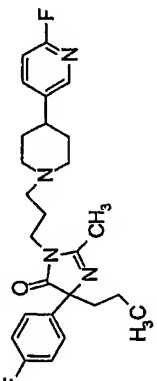
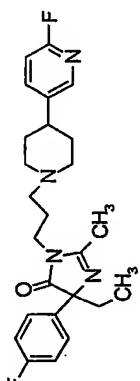
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
537		5,5-bis(4-fluorophenyl)-2-methyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2 & 16	489.30	1.81	
538		5,5-bis(4-fluorophenyl)-3-{3-[4-(6-fluoro-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2, 8, & 16	507.40	2.20	
539		5-(4-fluorophenyl)-3-{3-[4-(6-fluoro-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-5-dihydro-4H-imidazol-4-one	Example 2, 8, & 16			
540		5-ethyl-5-(4-fluorophenyl)-3-{3-[4-(6-fluoro-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one	Example 2, 8, & 16	441.40	1.79	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
541		3-{3-[4-(3,4-difluorophenyl)-1-piperidinyl]-2-hydroxypropyl}-5,5-bis(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2 & 16			
542		5-(4-fluorophenyl)-3-{3-[4-(6-fluoro-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-5-propyl-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2, 8, & 16	455.40	1.96	
543		5,5-bis(4-fluorophenyl)-3-{3-[4-(6-fluoro-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2 & 16	507.40	2.19	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
544		5-(4-fluorophenyl)-2-methyl-5-propyl-3-{3-[4-(3-pyridinyl)-1-piperidinyl]propyl}-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2, 8, & 16	437.30	1.28	
545		5,5-bis(4-fluorophenyl)-3-{3-[4-(6-methoxy-3-pyridinyl)-1-piperidinyl]propyl}-2-methyl-3,5-dihydro-4H-imidazol-4-one hydrochloride	Example 2 & 16	519.60	1.32	
546		N-[3-(1-{3-[(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolyl)]propyl}(4-piperidyl))phenyl]-2-methylpropanamide, chloride	Example 8 & 16	507.53	3.18	

Table 1

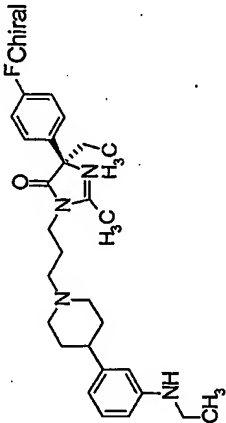
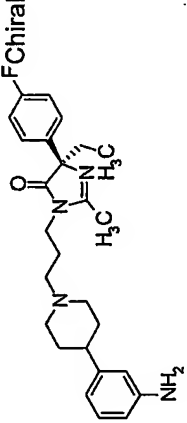
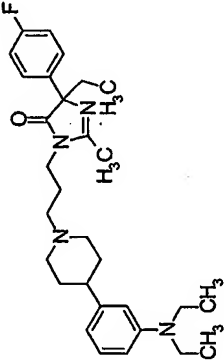
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
547		(4R)-4-ethyl-1-(3-(4-[3-(ethylamino)phenyl]piperidyl)propyl)-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 8	465.20	1.74	
548		(4R)-1-(3-[4-(3-aminophenyl)piperidyl]propyl)-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 8	437.56	1.41	
549		1-(3-(4-[3-(diethylamino)phenyl]piperidyl)propyl)-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 8	493.30	1.76	

Table 1

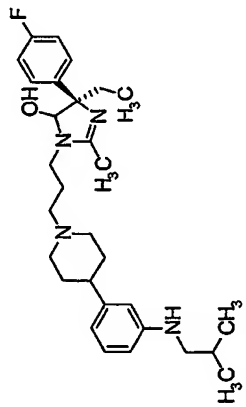
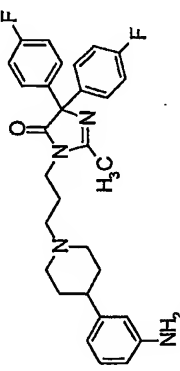
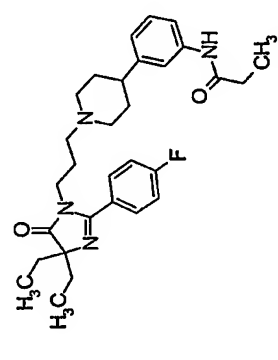
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
550		(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-1-[3-(4-{3-[(2-methylpropyl)amino]phenyl}piperidyl)propyl]-2-imidazolin-5-ol	Example 8 & 16	495.40	2.20	
551		1-[3-[4-(3-aminophenyl)piperidyl]propyl]-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 8	503.49	3.07	
552		N-[3-(1-{3-[4,4-diethyl-2-(4-fluorophenyl)-5-oxo-2-imidazolinyl]propyl}-4-piperidyl)phenyl]propanamide	Example 2 & 16	507.50	2.51	0.5; 10% MeOH / CH ₂ Cl ₂

Table 1

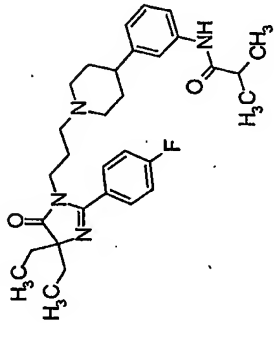
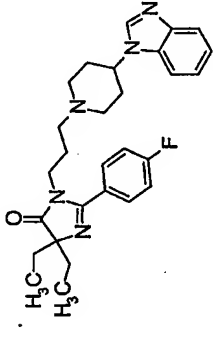
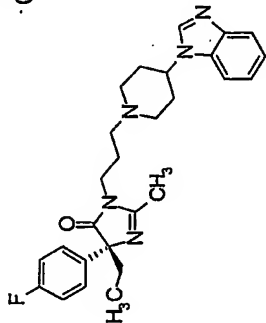
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
553		N-[3-(1-[3-[4,4-diethyl-2-(4-fluorophenyl)-5-oxo(2-imidazolyl)]propyl](4-piperidyl))phenyl]-2-methylpropanamide	Example 2 & 16	521.40	2.56	0.5; 10% MeOH / CH ₂ Cl ₂
554		1-[3-(4-benzimidazolylpiperidyl)propyl]-4,4-diethyl-2-(4-fluorophenyl)-2-imidazolin-5-one	Example 2	476.30	1.43	0.15; 5% MeOH / CH ₂ Cl ₂
555	 Chiral	(4R)-1-[3-(4-benzimidazolylpiperidyl)propyl]-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 5	462.20	1.56	0.125; 5% MeOH / CH ₂ Cl ₂

Table 1

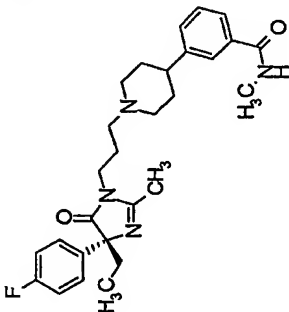
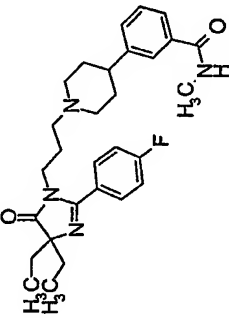
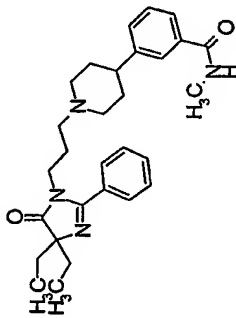
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
556	<p>Chiral</p> 	[3-(1-[3-(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolinyl)]propyl)(4-piperidyl))phenyl]-N-methylcarboxamide	Example 5	479.40	1.93	0.3; 10% MeOH / CH ₂ Cl ₂
557		[3-(1-[3-[4,4-diethyl-2-(4-fluorophenyl)-5-oxo(2-imidazolinyl)]propyl)(4-piperidyl))phenyl]-N-methylcarboxamide	Example 2	493.50	1.89	0.15; 5% MeOH / CH ₂ Cl ₂
558		(3-(1-[3-(4,4-diethyl-5-oxo-2-phenyl(2-imidazolinyl))propyl](4-piperidyl))phenyl)-N-methylcarboxamide	Example 2	475.30	1.83	0.15; 5% MeOH / CH ₂ Cl ₂

Table 1

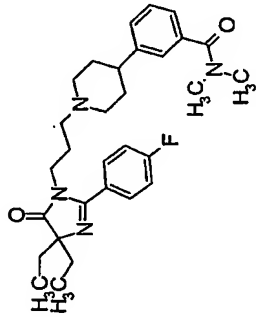
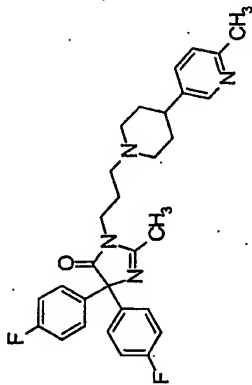
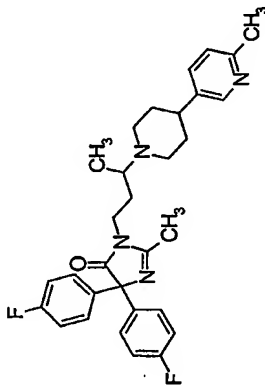
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
559		[3-(1-{3-[4,4-diethyl-2-(4-fluorophenyl)-5-oxo(2-imidazolinyl)]propyl}(4-piperidyl))phenyl]-N,N-dimethylcarboxamide	Example 2	507.50	1.97	0.17; 5% MeOH / CH ₂ Cl ₂
560		4,4-bis(4-fluorophenyl)-2-methyl-1-{3-[4-(6-methyl(3-pyridyl))piperidyl]propyl}-2-imidazolin-5-one	Example 2 & 16	503.20	1.74	0.3; 10% MeOH / CH ₂ Cl ₂
561		4,4-bis(4-fluorophenyl)-2-methyl-1-{3-[4-(6-methyl(3-pyridyl))piperidyl]butyl}-2-imidazolin-5-one	Example 4 & 16	517.10	1.84	0.28; 10% MeOH / CH ₂ Cl ₂

Table 1

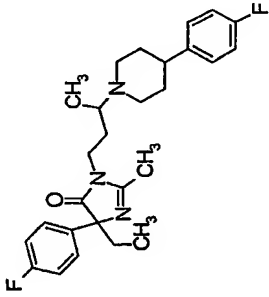
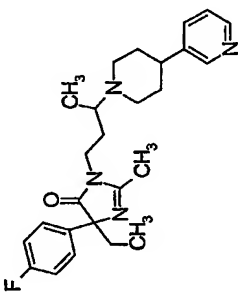
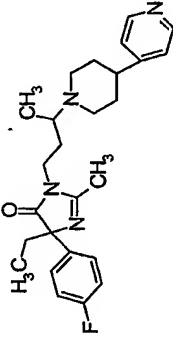
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
562		4-ethyl-4-(4-fluorophenyl)-1-{3-[4-(4-fluorophenyl)piperidyl]butyl}-2-methyl-2-imidazolin-5-one	Example 1	454.30	2.20	
563		4-ethyl-4-(4-fluorophenyl)-2-methyl-1-[3-(4-(3-pyridyl)piperidyl)butyl]-2-imidazolin-5-one	Example 1	437.20	1.00	
564		4-ethyl-4-(4-fluorophenyl)-2-methyl-1-[3-(4-(4-pyridyl)piperidyl)butyl]-2-imidazolin-5-one	Example 1	437.10	1.10	

Table 1

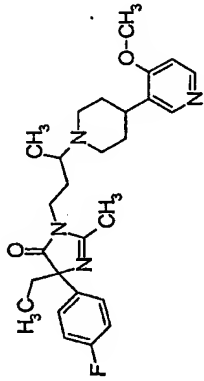
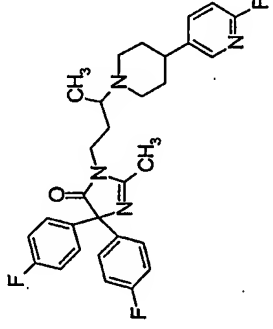
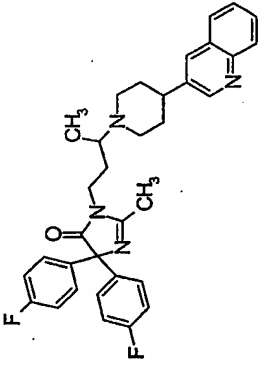
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
565		4-ethyl-4-(4-fluorophenyl)-1-{3-[4-(4-methoxy(3-pyridyl))piperidyl]butyl}-2-methyl-2-imidazolin-5-one	Example 1	467.20	1.15	
566		4,4-bis(4-fluorophenyl)-1-{3-[4-(6-fluoro(3-pyridyl))piperidyl]butyl}-2-methyl-2-imidazolin-5-one	Example 1	521.40	2.34	
567		4,4-bis(4-fluorophenyl)-2-methyl-1-[3-(4-(3-quinolyl)piperidyl)butyl]-2-imidazolin-5-one	Example 1	553.40	2.14	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
568		1-[3-(4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)propyl)-4-(4-fluorophenyl)-2-methyl-4-propyl-2-imidazolin-5-one	Example 1	480.40	2.27	
569		2-[3-(4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)propyl)-2,4-diaza-3-(4-fluorophenyl)spiro[4.4]non-3-en-1-one	Example 1	478.40	2.03	
570		2,4-diaza-3-(4-fluorophenyl)-2-[3-(4-(4-pyridyl)propyl)propyl]spiro[4.4]non-3-en-1-one	Example 1	435.30	0.82	

Table 1

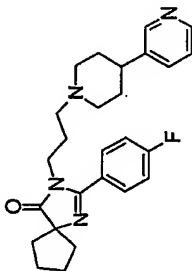
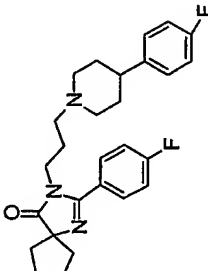
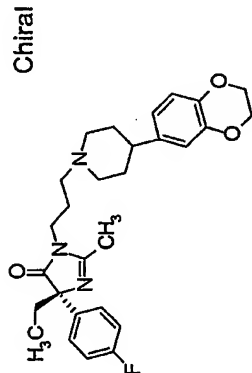
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
571		2,4-diaza-3-(4-fluorophenyl)-2-[3-(4-(3-pyridyl)piperidyl)propyl]spiro[4.4]non-3-en-1-one	Example 1	435.30	0.83	
572		2,4-diaza-3-(4-fluorophenyl)-2-[3-(4-(4-fluorophenyl)piperidyl)propyl]spiro[4.4]non-3-en-1-one	Example 1	452.40	2.07	
573		1-[3-(4-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)piperidyl)propyl]-(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 1	480.40	2.17	

Table 1

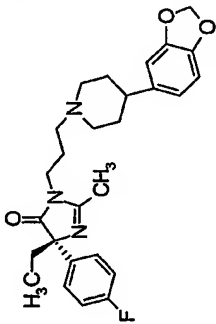
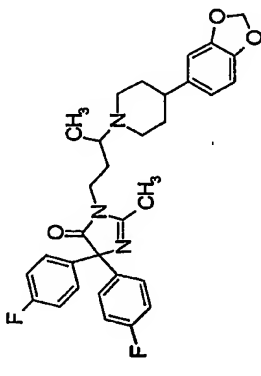
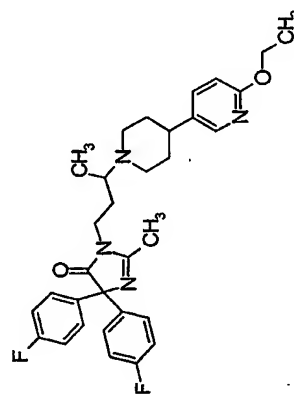
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
574	<p>Chiral</p> 	1-[3-(4-(2H-benzo[3,4-d][1,3-dioxolan-5-yl)piperidin-4-yl]butyl)-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 1	466.40	2.16	
575		1-[3-(4-(2H-benzo[3,4-d][1,3-dioxolan-5-yl)piperidin-4-yl]butyl)-4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 1	546.20	2.60	
576		4,4-bis(4-fluorophenyl)-1-{3-[4-(6-ethoxy(3-pyridyl))piperidin-2-butyl]-2-methyl-2-imidazolin-5-one	Example 1	547.20	2.46	

Table 1

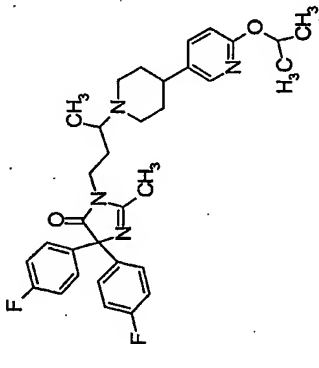
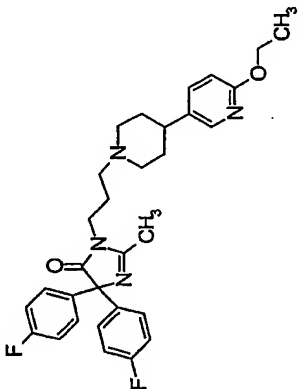
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
577		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-{4-[6-(methylethoxy)(3-pyridyl)]piperidyl}butyl)-2-imidazolin-5-one	Example 1	561.20	2.51	
578		4,4-bis(4-fluorophenyl)-1-[3-[4-(6-ethoxy(3-pyridyl)]piperidyl]propyl]-2-methyl-2-imidazolin-5-one	Example 1	533.20	2.40	

Table 1

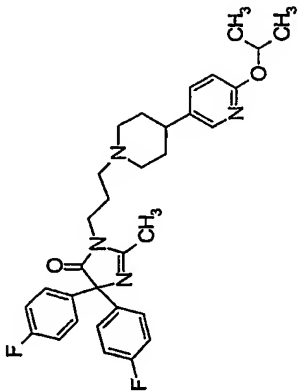
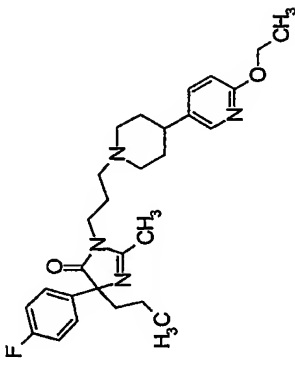
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
579		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-{4-[(methylethoxy)(3-pyridyl)]piperidyl}propyl)-2-imidazolin-5-one	Example 1	547.40	2.44	
580		1-{3-[4-(6-ethoxy(3-pyridyl))piperidyl]propyl}-4-(4-fluorophenyl)-2-methyl-4-propyl-2-imidazolin-5-one	Example 1	481.30	2.15	

Table 1

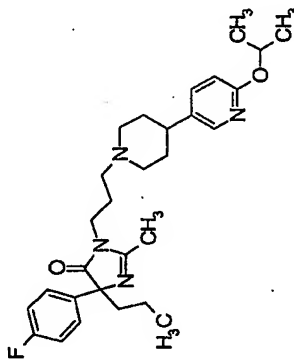
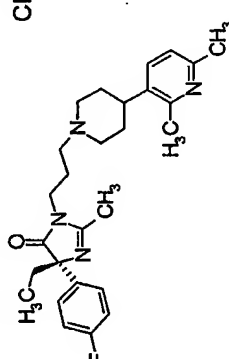
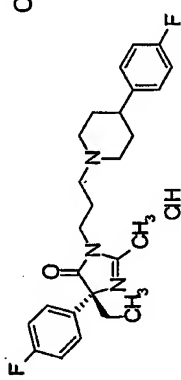
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
581		4-(4-fluorophenyl)-2-methyl-1-(3-{4-[6-(methylethoxy)(3-pyridyl)]piperidyl}propyl)-4-propyl-2-imidazolin-5-one	Example 1	495.30	2.23	
582		(4R)-1-(3-{4-[2,6-dimethyl(3-pyridyl)]piperidyl}propyl)-4-ethyl-4-(4-fluorophenyl)-2-imidazolin-5-one	Example 5	451.30	1.05	
583		(4R)-4-ethyl-4-(4-fluorophenyl)-1-(3-[4-(4-fluorophenyl)piperidyl]propyl)-2-methyl-2-imidazolin-5-one, chloride, chloride	Example 5			

Table 1

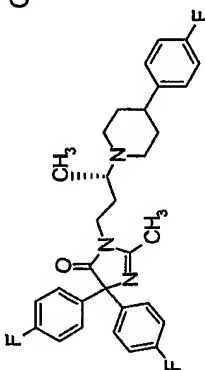
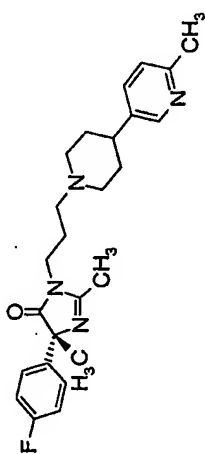
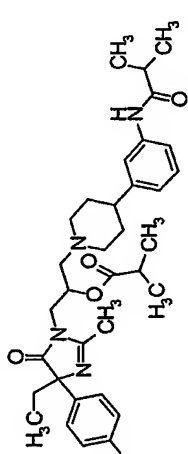
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
584	<p>Chiral</p>  <p>CH</p>	1-[(3S)-3-[4-(4-fluorophenyl)piperidin-1-yl]butyl]-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one, chloride	Example 4	520.20	2.49	
585		(4R)-4-(4-fluorophenyl)-2,4-dimethyl-1-[3-[4-(6-methyl(3-pyridyl))piperidin-2-yl]propyl]-2-imidazolin-5-one	Example 4 & 16	423.20	0.71	
586		1-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolyl)methyl]-2-[4-[3-(2-methylpropanoylamino)phenyl]piperidinylethyl] 2-methylpropanoate	Example 6	593.00	2.26	

Table 1

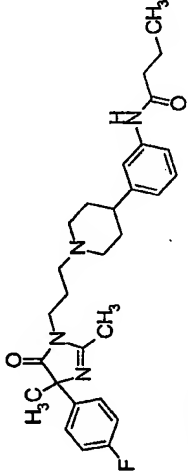
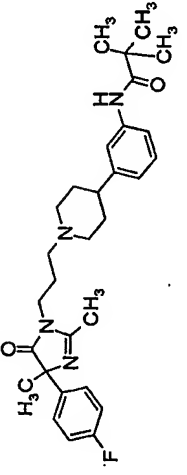
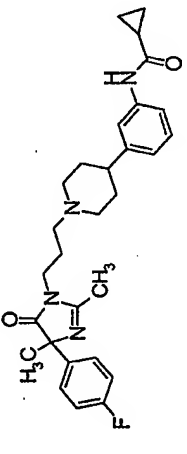
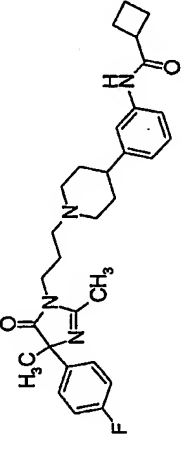
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
587		N-[3-(1-{3-[4-(4-fluorophenyl)-2,4-dimethyl-5-oxo-2-imidazolyl]propyl}-4-piperidyl)phenyl]butanamide	Example 6	493.50	2.03	
588		N-[3-(1-{3-[4-(4-fluorophenyl)-2,4-dimethyl-5-oxo(2-imidazolyl)]propyl}(4-piperidyl)phenyl]-2,2-dimethylpropanamide	Example 6	507.50	2.13	
589		cyclopropyl-N-[3-(1-{3-[4-(4-fluorophenyl)-2,4-dimethyl-5-oxo(2-imidazolyl)]propyl}(4-piperidyl)phenyl]carboxamide	Example 6	491.40	1.99	
590		cyclobutyl-N-[3-(1-{3-[4-(4-fluorophenyl)-2,4-dimethyl-5-oxo(2-imidazolyl)]propyl}(4-piperidyl)phenyl]carboxamide	Example 6	505.50	2.08	

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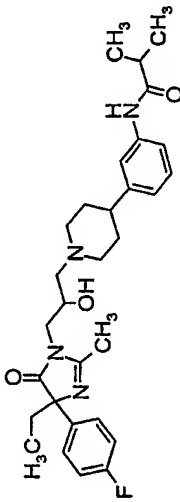
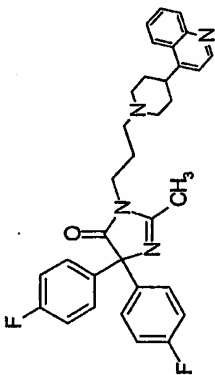
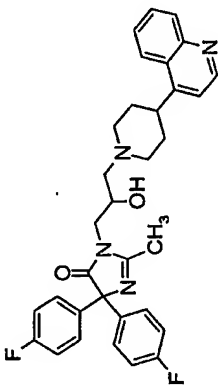
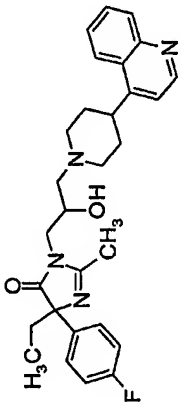
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
591		N-[3-(1-{3-[4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolyl)]-2-hydroxypropyl}(4-piperidyl))phenyl]-2-methylpropanamide	Example 6	523.20	2.11	
592		4,4-bis(4-fluorophenyl)-2-methyl-1-[3-(4-(4-quinolyl)piperidyl)propyl]-2-imidazolin-5-one	Example 26	539.40	1.98	
593		4,4-bis(4-fluorophenyl)-1-[2-hydroxy-3-(4-(4-quinolyl)piperidyl)propyl]-2-methyl-2-imidazolin-5-one	Example 6 & 26	555.40	1.94	
594		4-ethyl-4-(4-fluorophenyl)-1-[2-hydroxy-3-(4-(4-quinolyl)piperidyl)propyl]-2-methyl-2-imidazolin-5-one	Example 6 & 26	489.00	1.33	

Table 1

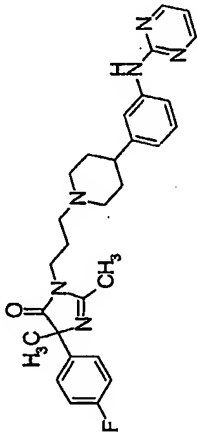
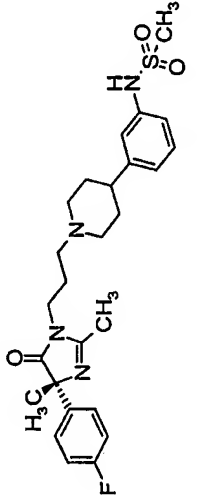
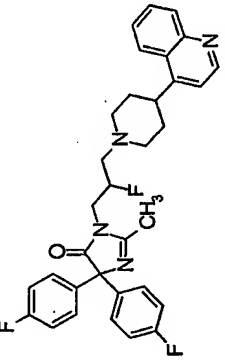
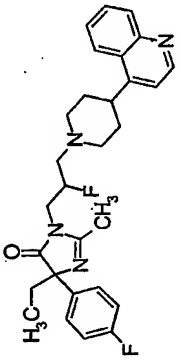
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
595		4-(4-fluorophenyl)-2,4-dimethyl-1-(3-(4-(3-(pyrimidin-2-ylamino)phenyl)piperidyl)propyl)-2-imidazolin-5-one	Example 30	501.20	2.07	
596		(4R)-4-(4-fluorophenyl)-2,4-dimethyl-1-(3-(4-(3-((methylsulfonyl)amino)phenyl)piperidyl)propyl)-2-imidazolin-5-one	Example 30	501.20	1.92	
597		4,4-bis(4-fluorophenyl)-1-[2-fluoro-3-(4-(4-quinolyl)piperidyl)propyl]-2-methyl-2-imidazolin-5-one	Example 7	557.00	2.04	
598		4-ethyl-1-[2-fluoro-3-(4-(4-quinolyl)piperidyl)propyl]-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 7	491.00	1.64	

Table 1

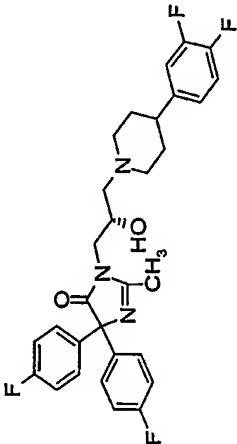
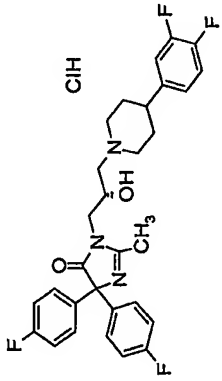
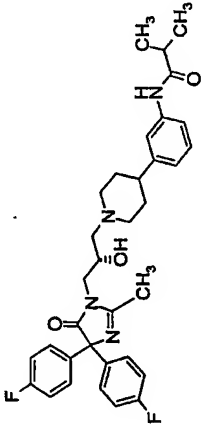
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
599		1-((2S)-3-[4-(3,4-difluorophenyl)piperidin-2-hydroxypropyl]-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 6	540.00	2.52	
600		1-((2S)-3-[4-(3,4-difluorophenyl)piperidin-2-hydroxypropyl]-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one, chloride	Example 6	540.10	2.53	
601		N-[3-(1-((2S)-3-[4,4-bis(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolinyl)]-2-hydroxypropyl)(4-piperidinyl)phenyl]-2-methylpropanamide	Example 6	589.20	2.40	

Table 1

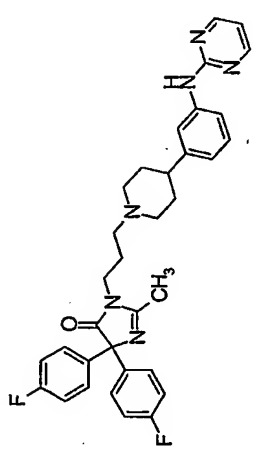
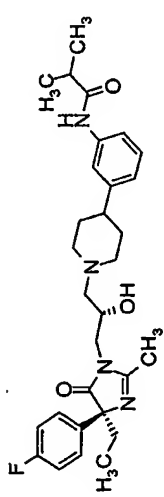
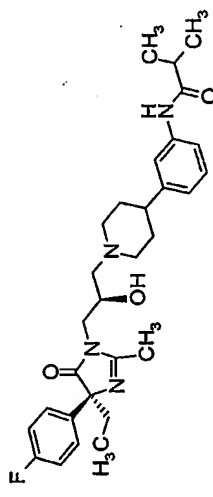
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
602		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-{4-[(pyrimidin-2-ylamino)phenyl]piperidyl}propyl)-2-imidazolin-5-one	Example 30	581.20	2.46	
603		N-[3-(1-[(2S)-3-[(4S)-4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolyl)]-2-hydroxypropyl](4-piperidyl))phenyl]-2-methylpropanamide	Example 6	523.00	2.10	
604		N-[3-(1-[(2R)-3-[(4S)-4-ethyl-4-(4-fluorophenyl)-2-methyl-5-oxo(2-imidazolyl)]-2-hydroxypropyl](4-piperidyl))phenyl]-2-methylpropanamide	Example 6	523.00	2.10	

Table 1

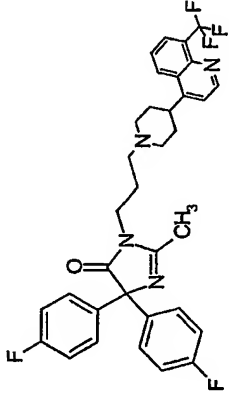
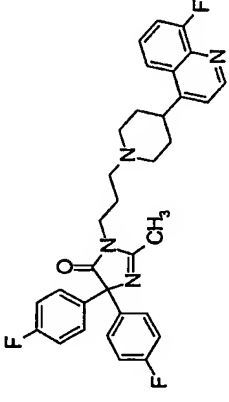
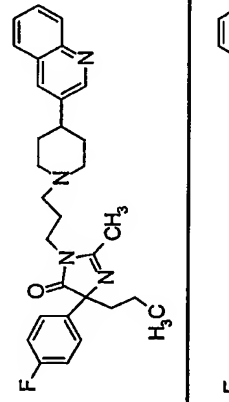
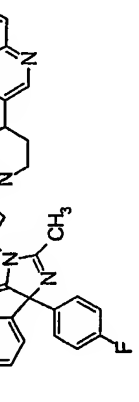
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
605		4,4-bis(4-fluorophenyl)-2-methyl-1-(3-(4-(8-(trifluoromethyl)(4-quinolyl))piperidyl)propyl)-2-imidazolin-5-one	Example 26 & 30	607.30	2.64	
606		4,4-bis(4-fluorophenyl)-1-(3-(4-(8-fluoro(4-quinolyl))piperidyl)propyl)-2-methyl-2-imidazolin-5-one	Example 26 & 30	557.20	2.32	
607		4-(4-fluorophenyl)-2-methyl-4-propyl-1-[3-(4-(3-quinolyl)piperidyl)propyl]-2-imidazolin-5-one	Example 2, 8, & 17	487.20	1.91	
608		4,4-bis(4-fluorophenyl)-2-methyl-1-[3-(4-(3-quinolyl)piperidyl)propyl]-2-imidazolin-5-one	Example 2, 8, & 17	539.40	2.11	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
609		(4R)-4-ethyl-4-(4-fluorophenyl)-2-methyl-1-{3-(4-(3-quinolyl)piperidyl)propyl}-2-imidazolin-5-one	Example 2, 8, & 17	473.20	1.77	
610		2-{3-[4-(3-aminophenyl)piperidyl]propyl}-2,4-diaza-3-(4-fluorophenyl)spiro[4.4]non-3-en-1-one	Example 2, 8, & 17	449.30	0.94	
611		2,4-diaza-2-{3-[4-(6-fluoro(3-pyridyl)piperidyl)propyl]-3-(4-fluorophenyl)spiro[4.4]non-3-en-1-one	Example 2, 8, & 17	453.40	1.68	
612		1-{3-[4-(6-amino(3-pyridyl)piperidyl)propyl]-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	504.40	1.89	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
613		(4R)-4-ethyl-4-(4-fluorophenyl)-1-{3-[4-(4-methoxy(3-pyridyl))piperidyl]propyl}-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	453.20	0.90	
614		(4S)-4-(4-(4-fluorophenyl)-2-methyl-4-propyl-1-[3-(4-(3-pyridyl)piperidyl)propyl]-2-imidazolin-5-one, chloride, chloride	Example 2, 8, & 17	437.20	1.00	
615		1-[3-(4-(2H,3H-benzo[3,4-e][1,4-dioxin-6-yl)piperidyl]propyl)-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	546.50	2.43	
616		1-[3-(4-(3a-hydroimidazo[1,2-a]pyridin-5-yl)piperidyl)propyl]-4,4-bis(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	528.40	1.84	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
617		(4R)-1-[3-[4-(6-ethoxy(3-pyridyl))piperidyl]propyl]-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	481.30	2.06	
618		(4R)-1-[3-[4-(6-ethoxy(3-pyridyl))piperidyl]propyl]-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	467.40	1.99	
619		(4R)-1-[3-[4-(6-amino(3-pyridyl))piperidyl]propyl]-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	438.30	0.92	
620		1-[3-[4-(6-amino(3-pyridyl))piperidyl]propyl]-4-(4-fluorophenyl)-2-methyl-4-propyl-2-imidazolin-5-one	Example 2, 8, & 17	452.30	1.26	
621		1-[3-(4-(3a-hydroimidazol[1,2-a]pyridin-5-yl))piperidyl]propyl]-4-(4-fluorophenyl)-2-methyl-4-propyl-2-imidazolin-5-one	Example 2, 8, & 17	476.20	1.58	

Table 1

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
622		(4R)-1-[3-(4-(3a-hydroimidazolol[1,2-a]pyridin-5-yl)piperidyl)propyl]-4-ethyl-4-(4-fluorophenyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	462.20	1.03	
623		4,4-bis(4-fluorophenyl)-1-[3-[4-(2,6-dimethyl-3-pyridyl)piperidyl]propyl]-2-methyl-2-imidazolin-5-one	Example 2, 8, & 17	517.30	1.90	
624		1-[3-[4-(2,6-dimethyl-3-pyridyl)piperidyl]propyl]-4-(4-fluorophenyl)-2-methyl-4-propyl-2-imidazolin-5-one	Example 2, 8, & 17	465.30	1.37	
625		4,4-bis(4-fluorophenyl)-1-(3-[4-(3-(hydroxyethyl)phenyl)piperidyl]propyl)-2-methyl-2-imidazolin-5-one	Example 2, 8, & 11	532.30	1.23	

Table 1

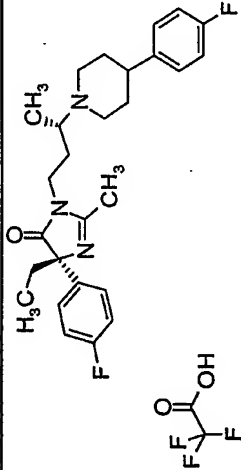
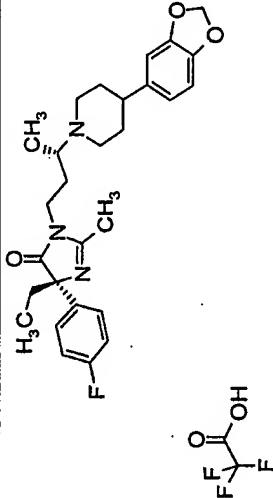
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
626		(5R)-5-ethyl-5-(4-fluorophenyl)-3-((3S)-3-[4-(4-fluorophenyl)-1-piperidinyl]butyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	454.30	2.31	
627		(5R)-3-((3S)-3-[4-(1,3-benzodioxol-5-yl)-1-piperidinyl]butyl)-5-ethyl-5-(4-fluorophenyl)-2-methyl-3,5-dihydro-4H-imidazol-4-one trifluoroacetate	Example 1	480.30	2.26	

Table 2

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
628		5,5-Bis-(4-fluoro-phenyl)-2-[3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl]-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 9	492.52	2.74	0.54 MeOH:EtOAc 4:6
629		5,5-Bis(4-fluorophenyl)-2-[3-[4-spiro-(1-phthalan)-1-piperidinyl]propyl]-3,5-dihydro-4H-imidazol-4-one; compound with trifluoro-acetic acid	Example 9	502.49	2.37	0.58 MeOH:EtOAc 4:6
630		5,5-Bis-(4-bromo-phenyl)-2-[3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl]-3,5-dihydro-imidazol-4-one	Example 9	614.35	2.59	0.53 MeOH:EtOAc 4:6

Table 2

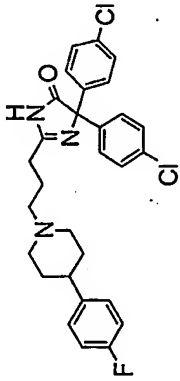
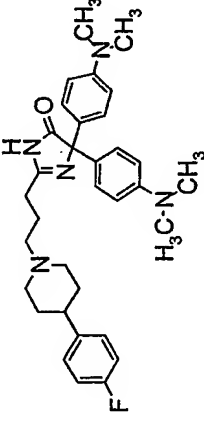
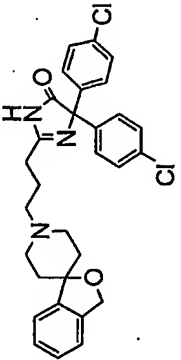
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
631		5,5-Bis-(4-chloro-phenyl)-2-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 9	524.45	2.56	0.52 MeOH:EtOAc 4:6
632		5,5-Bis-(4-dimethylamino-phenyl)-2-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 9	542.59	1.86	0.26 MeOH:EtOAc 4:6
633		5,5-Bis(4-chlorophenyl)-2-{3-[4-(spiro-(1-phthalan)-1-piperidinyl)propyl]}3,5-dihydro-4H-imidazol-4-one	Example 9	534.47	2.56	0.16 MeOH:EtOAc 2:8

Table 2

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
634		5,5-Bis(4-dimethylaminophenyl)-2-(3-{4-spiro(1-phthalan)-1-piperidinyl}propyl)-3,5-dihydro-4H-imidazol-4-one	Example 9	552.63	2.30	0.35 MeOH:EtOAc 4:6
635		5,5-Bis-(4-fluoro-phenyl)-2-(3-piperidin-1-yl-propyl)-3,5-dihydro-imidazol-4-one	Example 9	398.53	2.85	0.26 MeOH:EtOAc 4:6
636		2-(3-{4-(4-Trifluoromethyl-phenyl)-piperidin-1-yl}propyl)-1,3-diazaspiro[4.4]non-1-en-4-one	Example 9	408.53	2.59	0.26 MeOH:EtOAc 4:6

Table 2

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
637		5-Phenyl-5-trifluoromethyl-2-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 9	498.53	2.81	0.58 MeOH:EtOAc 2:8
638		4-[4,4-Bis-(4-fluoro-phenyl)-2-methyl-5-oxo-4,5-dihydro-imidazol-1-yl]-2-[4-(4-fluoro-phenyl)-piperidin-1-yl]-butyric acid methyl ester	Example 9	427.54	2.67	0.20 MeOH:EtOAc 4:6
639		2-{3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-propyl}-1,3-diaza-spiro[4.4]non-1-en-4-one	Example 9	358.46	2.56	0.32 MeOH:EtOAc 6:4

Table 2

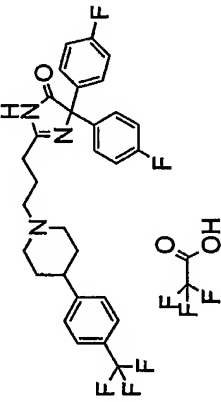
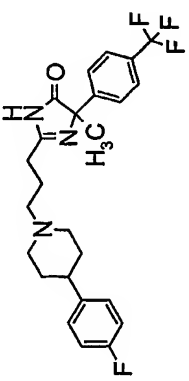
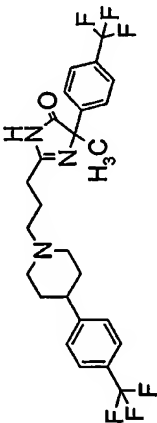
Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
640		5,5-Bis-(4-fluoro-phenyl)-2-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one; compound with trifluoro-acetic acid	Example 9	542.52	2.78	0.56 MeOH:EtOAc 4:6
641		2-{3-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-propyl}-5-methyl-5-(4-trifluoromethyl-phenyl)-3,5-dihydro-imidazol-4-one	Example 9	462.45	2.78	0.47 MeOH:EtOAc 4:6
642		5-Methyl-5-(4-(4-trifluoromethyl-phenyl)-2-{3-[4-(4-trifluoromethyl-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 9	512.44	2.89	0.41 MeOH:EtOAc 4:6

Table 2

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
643		5-(4-Chloro-phenyl)-2-[3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl]-5-methyl-3,5-dihydro-imidazol-4-one	Example 9	428.41	2.67	0.35 MeOH:EtOAc 4:6
644		5-(4-Chloro-phenyl)-2-[4-[4-(4-fluoro-phenyl)-piperidin-1-yl]-butyl]-5-methyl-3,5-dihydro-imidazol-4-one	Example 9	442.45	2.67	0.23 MeOH:EtOAc 4:6
645		2-[4-[4-(4-Fluoro-phenyl)-piperidin-1-yl]-butyl]-5-methyl-5-(4-trifluoromethyl-phenyl)-3,5-dihydro-imidazol-4-one	Example 9	476.47	2.78	0.26 MeOH:EtOAc 4:6

Table 2

Entry No.	Structure	Chemical Name	Prep Method	LC-MS [M+H] ⁺	HPLC RT (min)	TLC R _f
646		5-Ethyl-5-(4-fluoro-phenyl)-2-{3-[4-(4-fluoro-phenyl)-piperidin-1-yl]-propyl}-3,5-dihydro-imidazol-4-one	Example 9	426.47	2.56	0.48 MeOH:EtOAc 6:4
647		5-Ethyl-5-(4-fluoro-phenyl)-2-{3-[(3,4'-bipyridin-1'-yl)-propyl]-3,5-dihydro-imidazol-4-one	Example 9	409.47	0.25	0.21 MeOH:EtOAc 6:4

[203] The present invention relates to the use of the compounds of this invention for the treatment of bulimia and obesity including associated dyslipidemia and other obesity- and overweight-related complications such as, for example, cholesterol gallstones, cancer (e.g., colon, rectum, prostate, breast, ovary, endometrium, cervix, gallbladder, and bile duct), menstrual abnormalities, infertility, polycystic ovaries, osteoarthritis, and sleep apnea, as well as for a number of other pharmaceutical uses associated therewith, such as the regulation of appetite and food intake, dyslipidemia, hypertriglyceridemia, Syndrome X, type 1 and type 2 diabetes (non-insulin-dependent diabetes), maturity-onset diabetes of the young (MODY), latent autoimmune diabetes adult (LADA), impaired glucose tolerance (IGT), impaired fasting glucose (IFG), gestational diabetes atherosclerotic diseases such as heart failure, hyperlipidemia, hypercholesterolemia, low HDL levels, hypertension, cardiovascular disease (including atherosclerosis, coronary heart disease, coronary artery disease, and hypertension), cerebrovascular disease and peripheral vessel disease. The compounds of this invention may also be useful for treating physiological disorders related to, for example, regulation of insulin sensitivity, inflammatory response, plasma triglycerides, HDL, LDL, and cholesterol levels, and the like.

[204] The compounds of Formulae (Ia) and (Ib) of this invention are expected to be valuable as therapeutic agents. Accordingly, an embodiment of this invention includes a method of treating the various conditions identified above in a patient (including mammals) which comprises administering to said patient a composition containing an amount of the compound of Formulae (Ia) or (Ib) that is effective in treating the target condition.

[205] Compounds of Formulae (Ia) and (Ib) may be administered alone or in combination with one or more additional therapeutic agents. Combination therapy includes administration of a single pharmaceutical dosage formulation which contains a compound of Formulae (Ia) or (Ib) and one or more additional therapeutic agents, as well as administration of the compound of Formulae (Ia) or (Ib) and each additional therapeutic agents in its own separate pharmaceutical dosage formulation. For example, a compound of Formulae (Ia) or (Ib) and a therapeutic agent may be administered to the patient together in a single oral dosage composition such as a tablet or capsule, or each agent may be administered in separate oral dosage formulations.

[206] Where separate dosage formulations are used, the compound of Formulae (Ia) or (Ib) and one or more additional therapeutic agents may be administered at essentially the same time (e.g., concurrently) or at separately staggered times (e.g., sequentially).

[207] For example, the compounds of Formulae (Ia) and (Ib) may be used in combination with other therapies and drugs useful for the treatment of obesity, for example, in combination with β_3 -adrenoreceptor agonists such as CL-316,243, CB-1 antagonists, appetite suppressants, such as, for example, sibutramine (Meridia), and lipase inhibitors, such as, for example, orlistat (Xenical), or in

combination with a drug compound that modulates digestion and/or metabolism such as drugs that modulate thermogenesis, lipolysis, gut motility, fat absorption, and satiety.

[208] In addition, the compounds of Formula I may be administered in combination with one or more of the following hypoglycemic agents for the treatment of diabetes or diabetes-related disorders: insulin; biguanidines such as metformin or buformin; sulfonylureas such as acetohexamide, chlorpropamide, tolazamide, tolbutamide, glyburide, glipizide, glyclazide; or any other insulin secretagogue such as, for example, repaglinide and nateglinide; α -glycosidase inhibitors such as acarbose, voglibose, or miglitol; non-sulfonylurea secretagogues; insulin sensitizers such as thiazolidinediones and non-thiazolidinediones; PPAR agonists; hepatic glucose output lowering compounds; and β_3 -adrenoreceptor agonists. PPAR agonist may include agonists of PPAR- α , PPAR- γ , PPAR- δ or any combination of two or three of the subunits of PPAR. PPAR agonists include, for example, rosiglitazone and pioglitazone. Non-sulfonylurea drugs include, for example, GLP-1, GIP, secretin, nateglinide, meglitinide, repaglinide, glibenclamide, glimepiride, chlorpropamide, glipizide. GLP-1 includes derivatives of GLP-1 with longer half-lives than native GLP-1, such as, for example, fatty-acid derivatized GLP-1 and exendin.

[209] Also, the compounds of Formula I may be used in combination with HMG Co-A reductase inhibitors (statins), bile acid binding resin, or fibrin acid derivatives to improve the lipid profile of subjects with dyslipidemia. Compounds of Formula I may also be used in combination with agents that regulate hypertension (e.g., inhibitors of angiotension converting enzyme (ACE), β -blockers, calcium channel blockers).

[210] Furthermore, the compounds of this invention may have utility for the treatment of any of various CNS (central nervous system) or psychological disorders, such as the treatment of substance or behavioral addiction, and the treatment of disorders associated with the use of psychotropic substances. Likewise, the compounds of this invention may have utility for the management and treatment of cognition and memory disorders.

[211] The compounds of Formula (Ia) and (Ib) may also be utilized, in free base form or in compositions, as well as in research and diagnostics or as analytical reference standards, and the like, which are well known in the art. Therefore, the present invention includes compositions which are comprised of an inert carrier and an effective amount of a compound of Formula (Ia) or (Ib), or a salt, or ester thereof. An inert carrier is any material which does not interact with the compound to be carried and which lends support, means of conveyance, bulk, traceable material, and the like to the compound to be carried. An effective amount of the compound is that amount which produces a result or exerts an influence on the particular procedure being performed.

[212] It is anticipated that prodrug forms of the compounds of this invention will prove useful in certain circumstances, and such compounds are also intended to fall within the scope of the invention. Prodrug forms may have advantages over the parent compounds exemplified herein, in that they are better absorbed, better distributed, more readily penetrate the central nervous system, are more slowly metabolized or cleared, etc. Prodrug forms may also have formulation advantages in terms of crystallinity or water solubility. For example, compounds of the invention having one or more hydroxyl groups may be converted to esters or carbonates bearing one or more carboxyl, hydroxyl or amino groups, which are hydrolyzed at physiological pH values or are cleaved by endogenous esterases or lipases *in vivo*. See for example U.S. Patent Nos. 4,942,184; 4,960,790; 5,817,840; and 5,824,701 (all of which are incorporated herein by reference in their entirety), and references therein.

[213] As used herein, various terms are defined below.

[214] When introducing elements of the present invention or the preferred embodiment(s) thereof, the articles "a," "an," "the," and "said" are intended to mean that there are one or more of the elements. The terms "comprising," "including," and "having" are intended to be inclusive and mean that there may be additional elements other than the listed elements.

[215] The term "subject" as used herein includes mammals (e.g., humans and animals).

[216] The term "treatment" includes any process, action, application, therapy, or the like, wherein a subject, including a human being, is provided medical aid with the object of improving the subject's condition, directly or indirectly, or slowing the progression of a condition or disorder in the subject.

[217] The term "combination therapy" or "co-therapy" means the administration of two or more therapeutic agents to treat a diabetic condition and/or disorder. Such administration encompasses co-administration of two or more therapeutic agents in a substantially simultaneous manner, such as in a single capsule having a fixed ratio of active ingredients or in multiple, separate capsules for each inhibitor agent. In addition, such administration encompasses use of each type of therapeutic agent in a sequential manner.

[218] The phrase "therapeutically effective" means the amount of each agent administered that will achieve the goal of improvement in a diabetic condition or disorder severity, while avoiding or minimizing adverse side effects associated with the given therapeutic treatment.

[219] The term "pharmaceutically acceptable" means that the subject item is appropriate for use in a pharmaceutical product.

[220] An object of this invention is to provide a method of inducing weight loss in an individual by administration of a compound of the invention. The method of the invention comprises

administering to an individual a therapeutically effective amount of at least one compound of the invention, or a prodrug thereof, which is sufficient to induce weight loss. The invention further comprises a method of preventing weight gain in an individual by administering an amount of at least one compound of the invention, or a prodrug thereof, which is sufficient to prevent weight gain.

[221] Based on well known assays used to determine the efficacy for treatment of conditions identified above in mammals, and by comparison of these results with the results of known medicaments that are used to treat these conditions, the effective dosage of the compounds of this invention can readily be determined for treatment of each desired indication. The amount of the active ingredient (e.g., compounds) to be administered in the treatment of one of these conditions can vary widely according to such considerations as the particular compound and dosage unit employed, the mode of administration, the period of treatment, the age and sex of the patient treated, and the nature and extent of the condition treated.

[222] The total amount of the active ingredient to be administered may generally range from about 0.0001 mg/kg to about 200 mg/kg, and preferably from about 0.01 mg/kg to about 200 mg/kg body weight per day. A unit dosage may contain from about 0.05 mg to about 1500 mg of active ingredient, and may be administered one or more times per day. The daily dosage for administration by injection, including intravenous, intramuscular, subcutaneous, and parenteral injections, and use of infusion techniques may be from about 0.01 to about 200 mg/kg. The daily rectal dosage regimen may be from 0.01 to 200 mg/kg of total body weight. The transdermal concentration may be that required to maintain a daily dose of from 0.01 to 200 mg/kg.

[223] Of course, the specific initial and continuing dosage regimen for each patient will vary according to the nature and severity of the condition as determined by the attending diagnostician, the activity of the specific compound employed, the age of the patient, the diet of the patient, time of administration, route of administration, rate of excretion of the drug, drug combinations, and the like. The desired mode of treatment and number of doses of a compound of the present invention may be ascertained by those skilled in the art using conventional treatment tests.

[224] The compounds of this invention may be utilized to achieve the desired pharmacological effect by administration to a patient in need thereof in an appropriately formulated pharmaceutical composition. A patient, for the purpose of this invention, is a mammal, including a human, in need of treatment for a particular condition or disease. Therefore, the present invention includes pharmaceutical compositions which are comprised of a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound. A pharmaceutically acceptable carrier is any carrier which is relatively non-toxic and innocuous to a patient at concentrations consistent with effective activity of the active ingredient so that any side effects ascribable to the carrier do not

vitate the beneficial effects of the active ingredient. A therapeutically effective amount of a compound is that amount which produces a result or exerts an influence on the particular condition being treated. The compounds described herein may be administered with a pharmaceutically-acceptable carrier using any effective conventional dosage unit forms, including, for example, immediate and timed release preparations, orally, parenterally, topically, or the like.

[225] For oral administration, the compounds may be formulated into solid or liquid preparations such as, for example, capsules, pills, tablets, troches, lozenges, melts, powders, solutions, suspensions, or emulsions, and may be prepared according to methods known to the art for the manufacture of pharmaceutical compositions. The solid unit dosage forms may be a capsule which can be of the ordinary hard- or soft-shelled gelatin type containing, for example, surfactants, lubricants, and inert fillers such as lactose, sucrose, calcium phosphate, and corn starch.

[226] In another embodiment, the compounds of this invention may be tableted with conventional tablet bases such as lactose, sucrose, and cornstarch in combination with binders such as acacia, cornstarch, or gelatin; disintegrating agents intended to assist the break-up and dissolution of the tablet following administration such as potato starch, alginic acid, corn starch, and guar gum; lubricants intended to improve the flow of tablet granulation and to prevent the adhesion of tablet material to the surfaces of the tablet dies and punches, for example, talc, stearic acid, or magnesium, calcium or zinc stearate; dyes; coloring agents; and flavoring agents intended to enhance the aesthetic qualities of the tablets and make them more acceptable to the patient. Suitable excipients for use in oral liquid dosage forms include diluents such as water and alcohols, for example, ethanol, benzyl alcohol, and polyethylene alcohols, either with or without the addition of a pharmaceutically acceptable surfactant, suspending agent, or emulsifying agent. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance tablets, pills or capsules may be coated with shellac, sugar or both.

[227] Dispersible powders and granules are suitable for the preparation of an aqueous suspension. They provide the active ingredient in admixture with a dispersing or wetting agent, a suspending agent, and one or more preservatives. Suitable dispersing or wetting agents and suspending agents are exemplified by those already mentioned above. Additional excipients, for example, those sweetening, flavoring and coloring agents described above, may also be present.

[228] The pharmaceutical compositions of this invention may also be in the form of oil-in-water emulsions. The oily phase may be a vegetable oil such as liquid paraffin or a mixture of vegetable oils. Suitable emulsifying agents may be (1) naturally occurring gums such as gum acacia and gum tragacanth, (2) naturally occurring phosphatides such as soy bean and lecithin, (3) esters or partial esters derived from fatty acids and hexitol anhydrides, for example, sorbitan monooleate, and (4) condensation products of said partial esters with ethylene oxide, for example,

polyoxyethylene sorbitan monooleate. The emulsions may also contain sweetening and flavoring agents.

[229] Oily suspensions may be formulated by suspending the active ingredient in a vegetable oil such as, for example, arachis oil, olive oil, sesame oil, or coconut oil; or in a mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent such as, for example, beeswax, hard paraffin, or cetyl alcohol. The suspensions may also contain one or more preservatives, for example, ethyl or *n*-propyl *p*-hydroxybenzoate; one or more coloring agents; one or more flavoring agents; and one or more sweetening agents such as sucrose or saccharin.

[230] Syrups and elixirs may be formulated with sweetening agents such as, for example, glycerol, propylene glycol, sorbitol, or sucrose. Such formulations may also contain a demulcent, and preservative, flavoring and coloring agents.

[231] The compounds of this invention may also be administered parenterally, that is, subcutaneously, intravenously, intramuscularly, or interperitoneally, as injectable dosages of the compound in a physiologically acceptable diluent with a pharmaceutical carrier which may be a sterile liquid or mixture of liquids such as water, saline, aqueous dextrose and related sugar solutions; an alcohol such as ethanol, isopropanol, or hexadecyl alcohol; glycols such as propylene glycol or polyethylene glycol; glycerol ketals such as 2,2-dimethyl-1,1-dioxolane-4-methanol, ethers such as poly(ethyleneglycol) 400; an oil; a fatty acid; a fatty acid ester or glyceride; or an acetylated fatty acid glyceride with or without the addition of a pharmaceutically acceptable surfactant such as a soap or a detergent, suspending agent such as pectin, carbomers, methycellulose, hydroxypropylmethylcellulose, or carboxymethylcellulose, or emulsifying agent and other pharmaceutical adjuvants.

[232] Illustrative of oils which can be used in the parenteral formulations of this invention are those of petroleum, animal, vegetable, or synthetic origin, for example, peanut oil, soybean oil, sesame oil, cottonseed oil, corn oil, olive oil, petrolatum, and mineral oil. Suitable fatty acids include oleic acid, stearic acid, and isostearic acid. Suitable fatty acid esters are, for example, ethyl oleate and isopropyl myristate. Suitable soaps include fatty alkali metal, ammonium, and triethanolamine salts and suitable detergents include cationic detergents, for example, dimethyl dialkyl ammonium halides, alkyl pyridinium halides, and alkylamine acetates; anionic detergents, for example, alkyl, aryl, and olefin sulfonates, alkyl, olefin, ether, and monoglyceride sulfates, and sulfosuccinates; nonionic detergents, for example, fatty amine oxides, fatty acid alkanolamides, and polyoxyethylenepolypropylene copolymers; and amphoteric detergents, for example, alkyl-beta-aminopropionates, and 2-alkylimidazoline quarternary ammonium salts, as well as mixtures.

[233] The parenteral compositions of this invention may typically contain from about 0.5% to about 25% by weight of the active ingredient in solution. Preservatives and buffers may also be

used advantageously. In order to minimize or eliminate irritation at the site of injection, such compositions may contain a non-ionic surfactant having a hydrophile-lipophile balance (HLB) of from about 12 to about 17. The quantity of surfactant in such formulation ranges from about 5% to about 15% by weight. The surfactant can be a single component having the above HLB or can be a mixture of two or more components having the desired HLB.

[234] Illustrative of surfactants used in parenteral formulations are the class of polyethylene sorbitan fatty acid esters, for example, sorbitan monooleate and the high molecular weight adducts of ethylene oxide with a hydrophobic base, formed by the condensation of propylene oxide with propylene glycol.

[235] The pharmaceutical compositions may be in the form of sterile injectable aqueous suspensions. Such suspensions may be formulated according to known methods using suitable dispersing or wetting agents and suspending agents such as, for example, sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethyl-cellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents which may be a naturally occurring phosphatide such as lecithin, a condensation product of an alkylene oxide with a fatty acid, for example, polyoxyethylene stearate, a condensation product of ethylene oxide with a long chain aliphatic alcohol, for example, heptadecaethyleneoxycetanol, a condensation product of ethylene oxide with a partial ester derived from a fatty acid and a hexitol such as polyoxyethylene sorbitol monooleate, or a condensation product of an ethylene oxide with a partial ester derived from a fatty acid and a hexitol anhydride, for example polyoxyethylene sorbitan monooleate.

[236] The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent. Diluents and solvents that may be employed are, for example, water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile fixed oils are conventionally employed as solvents or suspending media. For this purpose, any bland, fixed oil may be employed including synthetic mono or diglycerides. In addition, fatty acids such as oleic acid may be used in the preparation of injectables.

[237] A composition of the invention may also be administered in the form of suppositories for rectal administration of the drug. These compositions may be prepared by mixing the drug (e.g., compound) with a suitable non-irritation excipient which is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such material are, for example, cocoa butter and polyethylene glycol.

[238] Another formulation employed in the methods of the present invention employs transdermal delivery devices ("patches"). Such transdermal patches may be used to provide continuous or discontinuous infusion of the compounds of the present invention in controlled amounts. The

construction and use of transdermal patches for the delivery of pharmaceutical agents is well known in the art (*see, e.g.,* U.S. Patent No. 5,023,252, incorporated herein by reference). Such patches may be constructed for continuous, pulsatile, or on demand delivery of pharmaceutical agents.

[239] It may be desirable or necessary to introduce the pharmaceutical composition to the patient via a mechanical delivery device. The construction and use of mechanical delivery devices for the delivery of pharmaceutical agents is well known in the art. For example, direct techniques for administering a drug directly to the brain usually involve placement of a drug delivery catheter into the patient's ventricular system to bypass the blood-brain barrier. One such implantable delivery system, used for the transport of agents to specific anatomical regions of the body, is described in U.S. Patent No. 5,011,472, incorporated herein by reference.

[240] The compositions of the invention may also contain other conventional pharmaceutically acceptable compounding ingredients, generally referred to as carriers or diluents, as necessary or desired. Any of the compositions of this invention may be preserved by the addition of an antioxidant such as ascorbic acid or by other suitable preservatives. Conventional procedures for preparing such compositions in appropriate dosage forms can be utilized.

[241] Commonly used pharmaceutical ingredients which may be used as appropriate to formulate the composition for its intended route of administration include: acidifying agents, for example, but are not limited to, acetic acid, citric acid, fumaric acid, hydrochloric acid, nitric acid; and alkalinizing agents such as, but are not limited to, ammonia solution, ammonium carbonate, diethanolamine, monoethanolamine, potassium hydroxide, sodium borate, sodium carbonate, sodium hydroxide, triethanolamine, triethylamine.

[242] Other pharmaceutical ingredients include, for example, but are not limited to, adsorbents (e.g., powdered cellulose and activated charcoal); aerosol propellants (e.g., carbon dioxide, CCl_2F_2 , $\text{F}_2\text{ClC}-\text{CClF}_2$ and CClF_3); air displacement agents (e.g., nitrogen and argon); antifungal preservatives (e.g., benzoic acid, butylparaben, ethylparaben, methylparaben, propylparaben, sodium benzoate); antimicrobial preservatives (e.g., benzalkonium chloride, benzethonium chloride, benzyl alcohol, cetylpyridinium chloride, chlorobutanol, phenol, phenylethyl alcohol, phenylmercuric nitrate and thimerosal); antioxidants (e.g., ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, hypophosphorus acid, monothioglycerol, propyl gallate, sodium ascorbate, sodium bisulfite, sodium formaldehyde sulfoxylate, sodium metabisulfite); binding materials (e.g., block polymers, natural and synthetic rubber, polyacrylates, polyurethanes, silicones and styrene-butadiene copolymers); buffering agents (e.g., potassium metaphosphate, potassium phosphate monobasic, sodium acetate, sodium citrate anhydrous and sodium citrate dihydrate); carrying agents (e.g., acacia syrup, aromatic syrup, aromatic elixir,

cherry syrup, cocoa syrup, orange syrup, syrup, corn oil, mineral oil, peanut oil, sesame oil, bacteriostatic sodium chloride injection and bacteriostatic water for injection); chelating agents (e.g., edetate disodium and edetic acid); colorants (e.g., FD&C Red No. 3, FD&C Red No. 20, FD&C Yellow No. 6, FD&C Blue No. 2, D&C Green No. 5, D&C Orange No. 5, D&C Red No. 8, caramel and ferric oxide red); clarifying agents (e.g., bentonite); emulsifying agents (but are not limited to, acacia, cetomacrogol, cetyl alcohol, glyceryl monostearate, lecithin, sorbitan monooleate, polyethylene 50 stearate); encapsulating agents (e.g., gelatin and cellulose acetate phthalate); flavorants (e.g., anise oil, cinnamon oil, cocoa, menthol, orange oil, peppermint oil and vanillin); humectants (e.g., glycerin, propylene glycol and sorbitol); levigating agents (e.g., mineral oil and glycerin); oils (e.g., arachis oil, mineral oil, olive oil, peanut oil, sesame oil and vegetable oil); ointment bases (e.g., lanolin, hydrophilic ointment, polyethylene glycol ointment, petrolatum, hydrophilic petrolatum, white ointment, yellow ointment, and rose water ointment); penetration enhancers (transdermal delivery) (e.g., monohydroxy or polyhydroxy alcohols, saturated or unsaturated fatty alcohols, saturated or unsaturated fatty esters, saturated or unsaturated dicarboxylic acids, essential oils, phosphatidyl derivatives, cephalin, terpenes, amides, ethers, ketones and ureas); plasticizers (e.g., diethyl phthalate and glycerin); solvents (e.g., alcohol, corn oil, cottonseed oil, glycerin, isopropyl alcohol, mineral oil, oleic acid, peanut oil, purified water, water for injection, sterile water for injection and sterile water for irrigation); stiffening agents (e.g., cetyl alcohol, cetyl esters wax, microcrystalline wax, paraffin, stearyl alcohol, white wax and yellow wax); suppository bases (e.g., cocoa butter and polyethylene glycols (mixtures)); surfactants (e.g., benzalkonium chloride, nonoxynol 10, oxtoxynol 9, polysorbate 80, sodium lauryl sulfate and sorbitan monopalmitate); suspending agents (e.g., agar, bentonite, carbomers, carboxymethylcellulose sodium, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, kaolin, methylcellulose, tragacanth and veegum); sweetening e.g., aspartame, dextrose, glycerin, mannitol, propylene glycol, saccharin sodium, sorbitol and sucrose); tablet anti-adherents (e.g., magnesium stearate and talc); tablet binders (e.g., acacia, alginic acid, carboxymethylcellulose sodium, compressible sugar, ethylcellulose, gelatin, liquid glucose, methylcellulose, povidone and pregelatinized starch); tablet and capsule diluents (e.g., dibasic calcium phosphate, kaolin, lactose, mannitol, microcrystalline cellulose, powdered cellulose, precipitated calcium carbonate, sodium carbonate, sodium phosphate, sorbitol and starch); tablet coating agents (e.g., liquid glucose, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, methylcellulose, ethylcellulose, cellulose acetate phthalate and shellac); tablet direct compression excipients (e.g., dibasic calcium phosphate); tablet disintegrants (e.g., alginic acid, carboxymethylcellulose calcium, microcrystalline cellulose, polacrillin potassium, sodium alginate, sodium starch glycollate and starch); tablet glidants (e.g., colloidal silica, corn starch and talc); tablet lubricants (e.g., calcium stearate, magnesium stearate, mineral

oil, stearic acid and zinc stearate); tablet/capsule opaquants (e.g., titanium dioxide); tablet polishing agents (e.g., carnuba wax and white wax); thickening agents (e.g., beeswax, cetyl alcohol and paraffin); tonicity agents (e.g., dextrose and sodium chloride); viscosity increasing agents (e.g., alginic acid, bentonite, carbomers, carboxymethylcellulose sodium, methylcellulose, povidone, sodium alginate and tragacanth); and wetting agents (e.g., heptadecaethylene oxycetanol, lecithins, polyethylene sorbitol monooleate, polyoxyethylene sorbitol monooleate, and polyoxyethylene stearate).

[243] The compounds described herein may be administered as the sole pharmaceutical agent or in combination with one or more other pharmaceutical agents where the combination causes no unacceptable adverse effects. For example, the compounds of this invention can be combined with known anti-obesity, or with known antidiabetic or other indication agents, and the like, as well as with admixtures and combinations thereof.

[244] The compounds described herein may also be utilized, in free base form or in compositions, in research and diagnostics, or as analytical reference standards, and the like. Therefore, the present invention includes compositions which are comprised of an inert carrier and an effective amount of a compound identified by the methods described herein, or a salt or ester thereof. An inert carrier is any material which does not interact with the compound to be carried and which lends support, means of conveyance, bulk, traceable material, and the like to the compound to be carried. An effective amount of compound is that amount which produces a result or exerts an influence on the particular procedure being performed.

[245] Formulations suitable for subcutaneous, intravenous, intramuscular, and the like; suitable pharmaceutical carriers; and techniques for formulation and administration may be prepared by any of the methods well known in the art (*see, e.g.*, Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa., 20th edition, 2000).

[246] The following examples are presented to illustrate the invention described herein, but should not be construed as limiting the scope of the invention in any way.

[247] Capsule Formulation

A capsule formula is prepared from:

Compound of this invention	10 mg
Starch	109 mg
Magnesium stearate	1 mg

The components are blended, passed through an appropriate mesh sieve, and filled into hard gelatin capsules.

[248] Tablet Formulation

A tablet is prepared from:

Compound of this invention	25 mg
Cellulose, microcrystalline	200 mg
Colloidal silicon dioxide	10 mg
Stearic acid	5.0 mg

The ingredients are mixed and compressed to form tablets. Appropriate aqueous and non-aqueous coatings may be applied to increase palatability, improve elegance and stability or delay absorption.

[249] Sterile IV Solution

A mg/mL solution of the desired compound of this invention is made using sterile, injectable water, and the pH is adjusted if necessary. The solution is diluted for administration with sterile 5% dextrose and is administered as an IV infusion.

[250] Intramuscular suspension

The following intramuscular suspension is prepared:

Compound of this invention	50 µg/mL
Sodium carboxymethylcellulose	5 mg/mL
TWEEN 80	4 mg/mL
Sodium chloride	9 mg/mL
Benzyl alcohol	9 mg/mL

The suspension is administered intramuscularly.

[251] Hard Shell Capsules

A large number of unit capsules are prepared by filling standard two-piece hard gelatin capsules each with powdered active ingredient, 150 mg of lactose, 50 mg of cellulose, and 6 mg of magnesium stearate.

[252] Soft Gelatin Capsules

A mixture of active ingredient in a digestible oil such as soybean oil, cottonseed oil, or olive oil is prepared and injected by means of a positive displacement pump into molten gelatin to form soft gelatin capsules containing the active ingredient. The capsules are washed and dried. The active

ingredient can be dissolved in a mixture of polyethylene glycol, glycerin and sorbitol to prepare a water miscible medicine mix.

[253] Immediate Release Tablets/Capsules

These are solid oral dosage forms made by conventional and novel processes. These units are taken orally without water for immediate dissolution and delivery of the medication. The active ingredient is mixed in a liquid containing ingredient such as sugar, gelatin, pectin, and sweeteners. These liquids are solidified into solid tablets or caplets by freeze drying and solid state extraction techniques. The drug compounds may be compressed with viscoelastic and thermoelastic sugars and polymers or effervescent components to produce porous matrices intended for immediate release, without the need of water.

[254] It should be apparent to one of ordinary skill in the art that changes and modifications can be made to this invention without departing from the spirit or scope of the invention as it is set forth herein.

Evaluation of Biological Activity

[255] Demonstration of the activity of the compounds of the present invention may be accomplished through *in vitro*, *ex vivo*, and *in vivo* assays that are well known in the art. For example, to demonstrate the efficacy of a pharmaceutical agent for the treatment of obesity and related disorders, the following assays may be used.

[256] Several animal models for testing the efficacy of compounds for treating obesity are available. For example, the following obesity and diabetic animal model systems can be used: ob mice (Coleman, *Dibetologia* 14:141-148, 1978; Chua et al., *Science* 271:994-996, 1996; Vaisse et al., *Nature Genet.* 14:95-100, 1996); db mice (Chen et al., *Cell* 84:491-495, 1996); agouti mice, and fatty rats (Takaga et al., *Biochem. Biophys. Res. Comm.* 225:75-83, 1996). For reviews, see for example, Friedman, et al., (*Mamm. Gen.* 1:130-144, 1991); Friedman and Liebel, (*Cell* 69:217-220, 1992). Test compounds are administered to these animals according to standard methods, and their effect on bodyweight is determined.

Evaluation of Compound's Efficacy on the Reduction of Food Intake in Lean Overnight Fasted Rats

Fasted-Refed Acute Feeding Assay

[257] The purpose of this protocol is to determine the effect of a single dose of an unknown compound on food consumption of lean overnight fasted rats. The fasted-refed rat model is frequently used in the field of obesity to identify compounds with potential for anorectic effects. This animal model has been successfully used in the identification and characterization of the

efficacy profile of compounds that are or have been used in the management of body weight in obese humans (*see, e.g.*, Balvet et al., Gen. Pharmacol. 13:293-297, 1982; Grignaschi et al., Br. J. Pharmacol. 127:1190-1194, 1999; McTavish and Heel, Drug 43:713-733, 1992; Rowland et al., Life Sci. 36:2295-2300, 1985).

[258] A typical study includes 60-80 male rats ($n=10/\text{treatment group}$) with an average body weight of approximately 280 g. Rats are kept in standard animal rooms under controlled temperature and humidity and a 12/12 light dark cycle. Rats are single-housed in suspended cages with a mesh floor. Water and food are continuously available unless the animals are being fasted for the study.

[259] The vehicle test: The rats are grouped based upon their performance on a vehicle test. The vehicle test is performed between 2 and 7 days before the efficacy test. The rats are fasted overnight during the dark phase (total of approx. 16-18 hrs). The animal is dosed with 0.5 mL deionized water. One hour after dosing, pre-weighed food jars are returned to the animal home cage. The rats are allowed one hour of feeding time. After 1 hour, the spillage is returned to the food jar and the amount of food consumed is determined. The rats are assigned to groups so that the mean and standard error of the mean of 1-hour food consumption are similar between groups.

[260] The efficacy test: The rats are fasted overnight during the dark phase (total of approx. 16-18 hr). The animal is dosed with an assigned treatment (2 mg/mL). One hour after dosing, pre-weighed food jars are returned to the cage. Food intake is recorded 30, 60, 90, 180, and 240 minutes post-food return. At each time point, spillage is returned to the food jar and then the food jars are weighed. The amount of food consumed is determined for each time point. Difference between treatment group is determined using appropriate statistical analysis.

Evaluation of Compound's Efficacy on the Reduction of Body Weight and Food and Water Consumption in Obese Zucker fa/fa Rats

Chronic Feeding Assay

[261] The purpose of this protocol is to determine the effect of chronic administration of an unknown compound on body weight and food and water consumption in obese Zucker fa/fa rats. Obese Zucker fa/fa rats are frequently used in the determination of compound efficacy in the reduction of body weight. This animal model has been successfully used in the identification and characterization of the efficacy profile of compounds that are or have been used in the management of body weight in obese humans (*see, e.g.*, Al-Barazani et al., Obes Res. 8:317-323, 2000; Assimacopoulos-Jeannet et al., Am. J. Physiol. 260(2 Pt 2):R278-283, 1991; Dryden et al., Horm. Metab. Res. 31:363-366, 1999; Edwards and Stevens, Pharmacol. Biochem. Behav. 47:865-872, 1994; Grinker et al., Pharmacol. Biochem. Behav. 12:265-275, 1980).

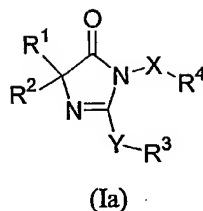
[262] A typical study includes 60-80 male Zucker fa/fa (n=10/treatment group) with an average body weight of approximately 550 g. Rats are kept in standard animal rooms under controlled temperature and humidity and a 12/12 light dark cycle. Water and food are continuously available. Rats are single-housed in large rat shoeboxes containing grid floor. Animals are adapted to the grid floors and sham-dosed with study vehicle for at least four days before the recording of two-days baseline measurement of body weight and 24-hr food and water consumption. Rats are assigned to one of 6-8 treatment groups based upon their body weight on baseline. The groups are set up so that the mean and standard error of the mean of body weight were similar.

[263] Animals are orally gavaged (2 mL/kg) daily before the dark phase of the LD/cycle for a pre-determined number of days (typically 6-14 days) with their assigned dose/compound. At this time, body weight, food and water consumption are measured. On the final day, animals are euthanized by CO₂ inhalation, and the body weight is measured.

[264] The structures, materials, compositions, and methods described herein are intended to be representative examples of the invention, and it will be understood that the scope of the invention is not limited by the scope of the examples. Those skilled in the art will recognize that the invention may be practiced with variations on the disclosed structures, materials, compositions and methods, and such variations are regarded as within the ambit of the invention.

We claim:

1. A compound of Formula (Ia)



wherein

R^1 and R^2 are independently selected from

(C₁-C₆)alkyl,

thienyl,

pyridyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)alkoxy,

(C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy, and

phenyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)alkoxy,

(C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy,

and

when R^1 and R^2 are each (C₁-C₆)alkyl, they can be taken together with the carbon atom to which they are attached to form a saturated 5- or 6-membered carbocyclic ring;

Y is (CH₂)_n;

n is 0 or 1;

R^3 is independently selected from

H,

(C₁-C₆)alkyl,

NR⁸R⁹,

(C₁-C₆)alkoxy,

(C₃-C₈)cycloalkyl,

pyridyl optionally substituted up to 3 times with (C₁-C₆)alkyl, (C₁-C₆)alkoxy, CN, halo,

(C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy,

phenyl optionally substituted up to 3 times with (C₁-C₆)alkyl, (C₁-C₆)alkoxy, CN, halo,

(C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy,

thienyl optionally substituted up to 3 times with (C₁-C₆)alkyl, (C₁-C₆)alkoxy, halo, or

(C₁-C₆)haloalkyl,

morpholinyl,

piperidyl, and

pyrolidinyl;

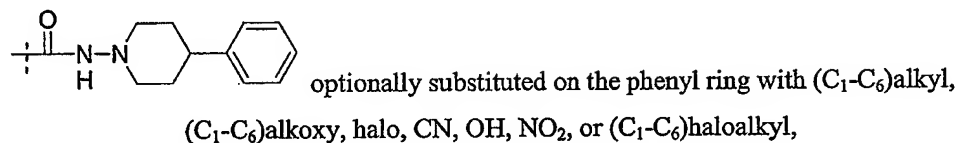
X is represents a linker selected from

a bond,

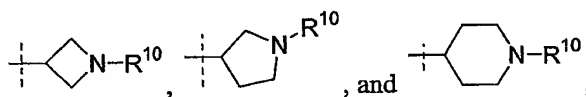
and

a (C₁-C₃)alkyl chain optionally substituted with F, OH, alkoxy, CO₂R⁵, C(O)R⁶, oxo, or C(O)NHR⁷;

R⁴ is selected from

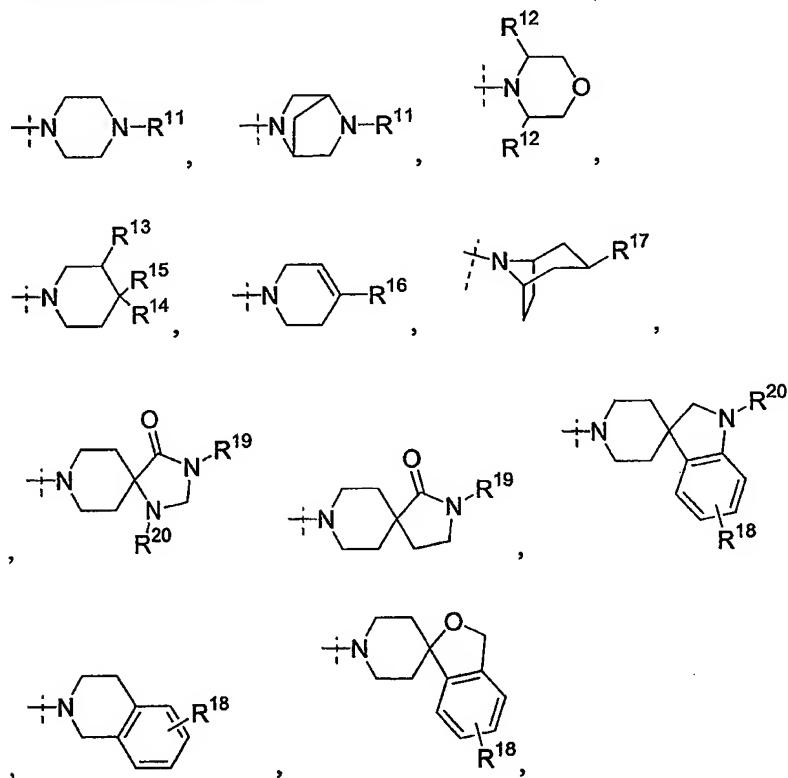


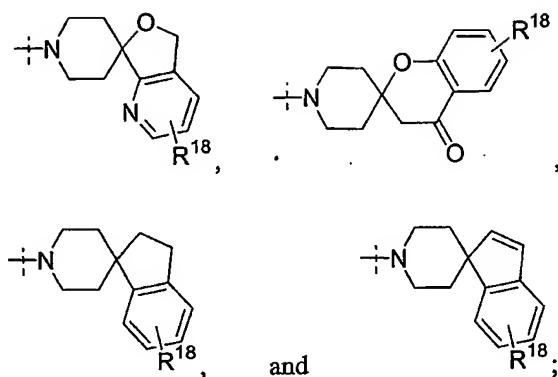
a 4-6-membered saturated heterocyclic ring selected from



and

a saturated or partially unsaturated, monocyclic, bicyclic, or spiroannulated heterocyclic ring radical selected from





R^5 is H or (C_1-C_6) alkyl;

R^6 is (C_3-C_8) cycloalkyl or (C_1-C_6) alkyl optionally substituted by phenyl;

R^7 is H or (C_1-C_6) alkyl;

R^8 and R^9 are independently selected from

H,

phenyl optionally substituted with CN, (C_1-C_6) alkyl, halo, (C_1-C_6) alkoxy, COR^6 ,

(C_1-C_6) haloalkyl, or NR^5R^7 ,

(C_3-C_8) cycloalkyl, and

(C_1-C_6) alkyl optionally substituted with halo, phenyl, (C_1-C_6) alkoxy, or OH;

R^{10} is selected from

H,

CO_2R^6 ,

(C_1-C_6) alkyl optionally substituted by

phenyl optionally substituted with (C_1-C_6) alkyl,

indolyl,

dihydrobenzofuryl or benzofuryl optionally substituted with halo,

benzothienyl optionally substituted with halo,

benzimidazolyl,

chromenyl optionally substituted with methoxy, nitro, oxo, hydroxy, halo, or

(C_1-C_6) alkyl,

methylenedioxyphenyl,

pyridyl, and

isoxazolyl optionally substituted with phenyl or (C_1-C_6) alkyl);

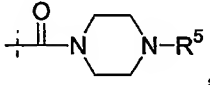
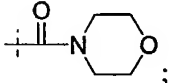
R¹¹ is selected from

H,
 pyrimidyl,
 (C₁-C₆)alkyl, and
 pyridyl optionally substituted with CN, (C₁-C₆)alkyl, halo, (C₁-C₆)alkoxy, COR⁶,
 (C₁-C₆)haloalkyl, or NR⁸R⁹, and
 phenyl optionally substituted with CN, (C₁-C₆)alkyl, halo, (C₁-C₆)alkoxy, COR⁶,
 (C₁-C₆)haloalkyl, or NR⁸R⁹;

R¹² is independently selected from

H, and
 (C₁-C₆)alkyl;

R¹³ is selected from

H,
 CON⁸R⁹,
 CO₂R⁵,
 CH₂OH,
, and
;

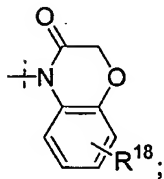
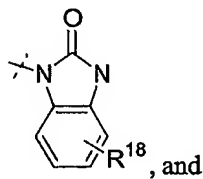
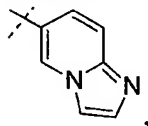
R¹⁴ is selected from

H,
 OH,
 COR⁶, and
 CN;

R¹⁵ is selected from

H,
 CO₂R⁵,
 (C₁-C₆)alkyl optionally substituted with one group selected from phenyl, OH, halo, and
 (C₁-C₆)alkoxy,
 phenyl optionally substituted with up to two groups independently selected from halo,

CO_2R^5 , NHCOR^6 , CONR^8R^9 , $(\text{C}_1\text{-C}_6)\text{alkyl}$ optionally substituted with OH, NR^5R^7 ,
 $(\text{C}_1\text{-C}_6)\text{alkoxy}$, NH-pyrimid-2-yl, $\text{NHSO}_2(\text{C}_1\text{-C}_6)\text{alkyl}$, NO_2 , CN,
 $(\text{C}_1\text{-C}_6)\text{haloalkoxy}$, and $(\text{C}_1\text{-C}_6)\text{haloalkyl}$,
 -O-phenyl optionally substituted with up to two groups selected from $(\text{C}_1\text{-C}_6)\text{alkyl}$,
 $(\text{C}_1\text{-C}_6)\text{haloalkoxy}$, $(\text{C}_1\text{-C}_6)\text{haloalkyl}$, halo and $(\text{C}_1\text{-C}_6)\text{alkoxy}$,
 C(O)phenyl optionally substituted with one group selected from halo, $(\text{C}_1\text{-C}_6)\text{alkyl}$, and
 $(\text{C}_1\text{-C}_6)\text{alkoxy}$,
 pyridyl optionally substituted on C with up to two groups selected from CN, CONHR^6 ,
 CO_2R^5 , $(\text{C}_1\text{-C}_6)\text{alkoxy}$, halo, OH, and $(\text{C}_1\text{-C}_6)\text{alkyl}$, and
 optionally substituted on N by oxo,
 naphthyl,
 benzodioxol-5-yl,
 1,2,4-oxadiazol-5-yl optionally substituted with pyridyl, phenyl, or $(\text{C}_1\text{-C}_6)\text{alkyl}$ optionally
 substituted with $(\text{C}_1\text{-C}_6)\text{alkoxy}$,
 1,2,4-oxadiazol-3-yl optionally substituted with $(\text{C}_1\text{-C}_6)\text{alkyl}$, pyridyl, or phenyl,
 benzotriazolyl,
 pyrimidyl optionally substituted with OR^5 , $(\text{C}_1\text{-C}_6)\text{alkyl}$, phenyl, or pyridyl,
 indolyl,
 benzimidazolyl,
 quinoliny optionally substituted with halo or CF_3 ,
 benzodioxanyl,



R^{16} is selected from

H,
 $(\text{C}_1\text{-C}_6)\text{alkyl}$,

phenyl optionally substituted with up to two groups independently selected from halo, CO_2R^5 , NHCOR^6 , CONR^8R^9 , $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, NH_2 , NO_2 , CN , and CF_3 , and

pyridyl optionally substituted with up to two groups independently selected from halo, CO_2R^5 , NHCOR^6 , CONR^8R^9 , $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, NH_2 , NO_2 , CN , and CF_3 ;

R^{17} is selected from

H,

$(\text{C}_1\text{-C}_6)\text{alkyl}$, and

phenyl optionally substituted with up to two groups independently selected from halo, CO_2R^5 , NHCOR^6 , CONR^8R^9 , $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, NH_2 , NO_2 , CN , and CF_3 ;

R^{18} is selected from H, halo, CN , $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, or $(\text{C}_1\text{-C}_6)\text{haloalkyl}$;

R^{19} is H, $(\text{C}_1\text{-C}_6)\text{alkyl}$, or phenyl;

R^{20} is selected from

H,

$\text{CO}_2(\text{C}_1\text{-C}_6)\text{alkyl}$ optionally substituted with phenyl($\text{CO}_2\text{-benzyl}$),

SO_2CH_3 , and

phenyl;

and pharmaceutically salts thereof.

2. The compound of claim 1, wherein

R^3 is independently selected from

H,

$(\text{C}_1\text{-C}_6)\text{alkyl}$,

NR^8R^9 ,

$(\text{C}_3\text{-C}_8)\text{cycloalkyl}$,

pyridyl optionally substituted up to 3 times with $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$, CN , halo, $(\text{C}_1\text{-C}_6)\text{haloalkyl}$, or $(\text{C}_1\text{-C}_6)\text{haloalkoxy}$,

phenyl optionally substituted up to 3 times with $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$,

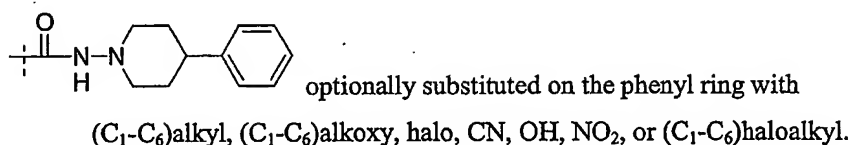
CN , halo, $(\text{C}_1\text{-C}_6)\text{haloalkyl}$, or $(\text{C}_1\text{-C}_6)\text{haloalkoxy}$,

thienyl optionally substituted up to 3 times with $(\text{C}_1\text{-C}_6)\text{alkyl}$, $(\text{C}_1\text{-C}_6)\text{alkoxy}$,

halo, or (C₁-C₆) haloalkyl;

X is a (C₁-C₅)alkyl chain optionally substituted with F, OH, alkoxy, CO₂R⁵, C(O)R⁶,
oxo, or C(O)NHR⁷; and

R⁴ is



3. The compound of claim 1, wherein

R³ is independently selected from

H,

(C₁-C₆)alkyl,

NR⁸R⁹,

(C₃-C₈)cycloalkyl,

pyridyl optionally substituted up to 3 times with (C₁-C₆)alkyl, (C₁-C₆)alkoxy, CN,

halo, (C₁-C₆)haloalkyl, or (C₁-C₆)haloalkoxy,

phenyl optionally substituted up to 3 times with (C₁-C₆)alkyl, (C₁-C₆)alkoxy,

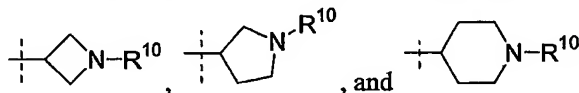
CN, halo, (C₁-C₆) haloalkyl, or (C₁-C₆)haloalkoxy,

thienyl optionally substituted up to 3 times with (C₁-C₆)alkyl, (C₁-C₆)alkoxy,

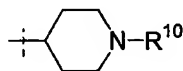
halo, or (C₁-C₆) haloalkyl;

X is a (C₁-C₅)alkyl chain optionally substituted with F, OH, alkoxy, CO₂R⁵, C(O)R⁶,
oxo, or C(O)NHR⁷; and

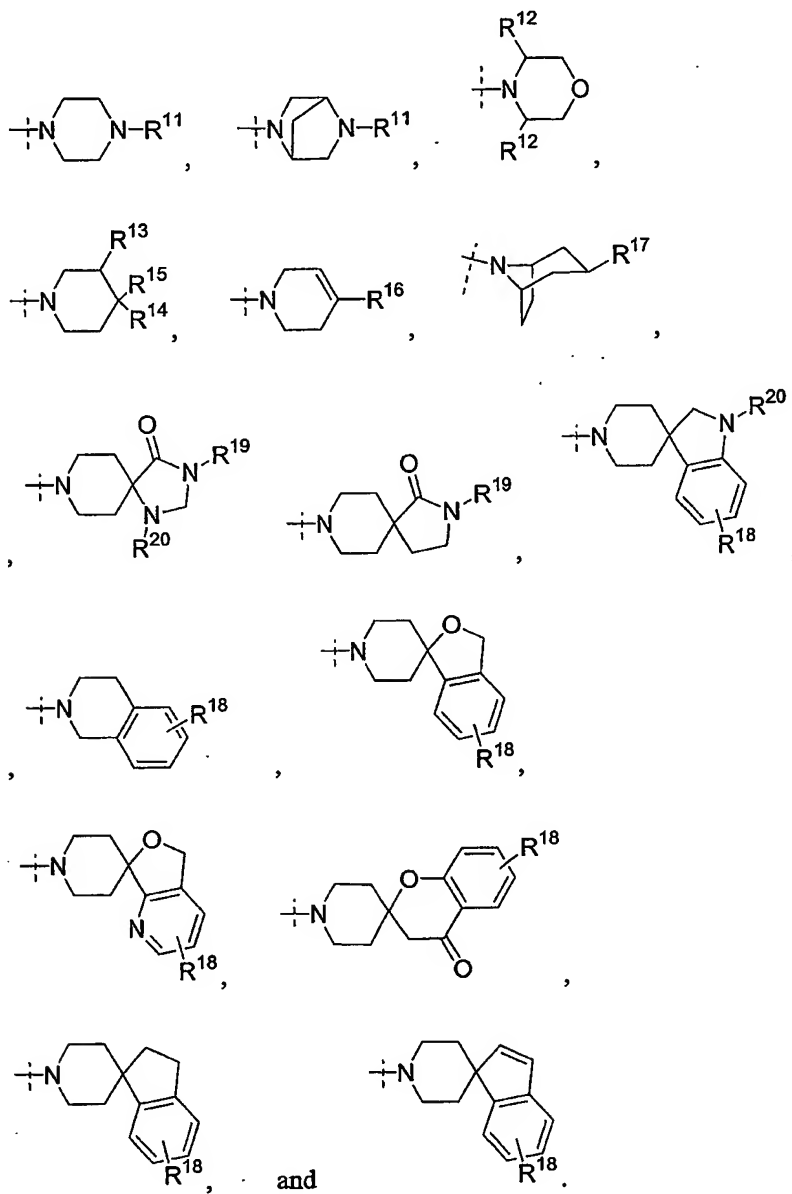
R⁴ is a 4-6-membered saturated heterocyclic ring selected from



4. The compound of claim 3, wherein R⁴ is



5. The compound of claim 1, wherein R^4 is a saturated or partially unsaturated, monocyclic, bicyclic, or spiroannulated heterocyclic ring radical selected from



6. The compound of claim 5, wherein

R^1 and R^2 are independently selected from

(C_1 - C_6)alkyl,

phenyl optionally substituted with halo, CN, (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy,

(C_1 - C_6)haloalkyl, or (C_1 - C_6)haloalkoxy,

and

when R^1 and R^2 are each (C_1 - C_6)alkyl, they can be taken together with the carbon atom to which they are attached to form a saturated 5- or 6-membered carbocyclic ring;

R^3 is independently selected from

H,

(C_1 - C_6)alkyl,

NR^8R^9 ,

(C_3 - C_8)cycloalkyl,

pyridyl optionally substituted up to 3 times with (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy, CN,

halo, (C_1 - C_6)haloalkyl, or (C_1 - C_6)haloalkoxy,

phenyl optionally substituted up to 3 times with (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy,

CN, halo, (C_1 - C_6) haloalkyl, or (C_1 - C_6)haloalkoxy,

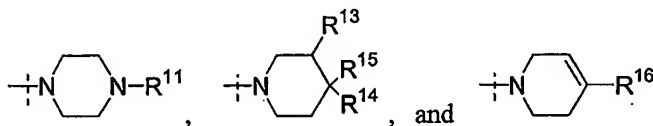
thienyl optionally substituted up to 3 times with (C_1 - C_6)alkyl, (C_1 - C_6)alkoxy,

halo, or (C_1 - C_6) haloalkyl;

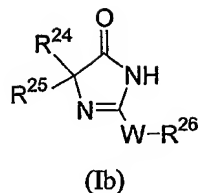
and

X is a (C_1 - C_3)alkyl chain optionally substituted with F, OH, alkoxy, CO_2R^5 , $C(O)R^6$, oxo, or $C(O)NHR^7$.

7. The compound of claim 6, wherein R^4 is selected from



8. A compound of Formula (Ib)



wherein

R^{24} and R^{25} are independently selected from

(C₁-C₆)alkyl,

thienyl,

pyridyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl,

(C₁-C₆)haloalkoxy, (C₁-C₆)alkoxy, and

phenyl optionally substituted with halo, CN, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl,

(C₁-C₆)haloalkoxy, (C₁-C₆)alkoxy,

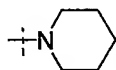
and

when R^{24} and R^{25} are each (C₁-C₆)alkyl, they can be taken together with the carbon atom to which they are attached to form a saturated 5- or 6-membered carbocyclic ring;

W is (CH₂)_p;

p is 3, 4, or 5;

R^{26} is selected from



optionally substituted with

phenyl optionally substituted with halo, CN, (C₁-C₆)haloalkoxy,

(C₁-C₆)haloalkyl, (C₁-C₆)alkyl, CH, (C₁-C₆)alkoxy, or

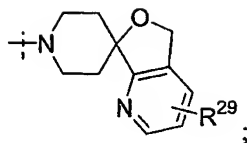
NR²⁷R²⁸,

pyridyl optionally substituted with halo, (C₁-C₆)haloalkyl,

(C₁-C₆)alkyl, CH, (C₁-C₆)alkoxy, NR²⁷R²⁸, or

up to three (C₁-C₆)alkyl groups,

and



R^{27} and R^{28} are independently selected from

H,

phenyl optionally substituted with CN, (C_1-C_6) alkyl, halo, (C_1-C_6) alkoxy,

$CO(C_1-C_6)$ alkyl, (C_1-C_6) haloalkyl, NH_2 , $N[(C_1-C_6)alkyl]_2$, or

$NH(C_1-C_6)alkyl$,

$(C_3-C_8)cycloalkyl$, and

$(C_1-C_6)alkyl$ optionally substituted with halo, phenyl, $(C_1-C_6)alkoxy$ or OH;

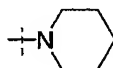
and

R^{29} is H, halo, CN, $(C_1-C_6)alkyl$, $(C_1-C_6)alkoxy$, or $(C_1-C_6)haloalkyl$;

and pharmaceutically salts thereof.

9. The compound of claim 8, wherein

R^{26} is



optionally substituted with

phenyl optionally substituted with halo, CN, $(C_1-C_6)haloalkoxy$,

$(C_1-C_6)haloalkyl$, $(C_1-C_6)alkyl$, CH, $(C_1-C_6)alkoxy$, or $NR^{27}R^{28}$,

pyridyl optionally substituted with halo, $(C_1-C_6)haloalkyl$,

$(C_1-C_6)alkyl$, CH, $(C_1-C_6)alkoxy$, $NR^{27}R^{28}$, or

up to three $(C_1-C_6)alkyl$ groups.

10. A pharmaceutical composition comprising an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.
11. A pharmaceutical composition comprising an effective amount of a compound of claim 8, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.
12. A pharmaceutical composition comprising an effective amount of a compound of claim 1,

or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier and one or more hypoglycemic agents.

13. The pharmaceutical composition of claim 12, wherein said hypoglycemic agent is selected from the group consisting of insulin, biguanidines, sulfonylureas, non-sulfonylurea secretagogues, insulin secretagogues, insulin sensitizers, α -glycosidase inhibitors, PPAR agonists, hepatic glucose output lowering compounds, and β_3 -adrenoreceptor agonists.
14. A pharmaceutical composition comprising an effective amount of a compound of claim 8, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier and one or more hypoglycemic agents.
15. The pharmaceutical composition of claim 14, wherein said hypoglycemic agent is selected from the group consisting of insulin, biguanidines, sulfonylureas, non-sulfonylurea secretagogues, insulin secretagogues, insulin sensitizers, α -glycosidase inhibitors, PPAR agonists, hepatic glucose output lowering compounds, and β_3 -adrenoreceptor agonists.
16. A pharmaceutical composition comprising an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier and one or more agents selected from the group consisting of HMG CoA reductase inhibitor, bile acid binding agent, fibric acid derivative, and agent that regulates hypertension.
17. A pharmaceutical composition comprising an effective amount of a compound of claim 8, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier and one or more agents selected from the group consisting of HMG CoA reductase inhibitor, bile acid binding agent, fibric acid derivative, and agent that regulates hypertension.
18. A pharmaceutical composition comprising an effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier and one or more agents selected from the group consisting of agents that modulate thermogenesis, lipolysis, gut motility, fat absorption, and satiety.
19. A pharmaceutical composition comprising an effective amount of a compound of claim 8, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier and one or more agents selected from the group consisting of agents that modulate thermogenesis, lipolysis, gut motility, fat absorption, and satiety.

20. A composition comprising an effective amount of a compound of claim 1, or a salt thereof, in combination with an inert carrier.
21. A composition comprising an effective amount of a compound of claim 8, or a salt thereof, in combination with an inert carrier.
22. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1.
23. The method of claim 22, wherein said obesity-related disorders include dyslipidemia, hypertriglyceridemia, hypertension, diabetes, Syndrome X, atherosclerotic disease, cardiovascular disease, cerebrovascular disease, peripheral vessel disease, cholesterol gallstones, cancer, menstrual abnormalities, infertility, polycystic ovaries, osteoarthritis, and sleep apnea.
24. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 8.
25. The method of claim 24, wherein said obesity-related disorders include dyslipidemia, hypertriglyceridemia, hypertension, diabetes, Syndrome X, atherosclerotic disease, cardiovascular disease, cerebrovascular disease, peripheral vessel disease, cholesterol gallstones, cancer, menstrual abnormalities, infertility, polycystic ovaries, osteoarthritis, and sleep apnea.
26. A method of regulating appetite and food intake comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1.
27. A method of regulating appetite and food intake comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 8.
28. A method of treating bulimia comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1.
29. A method of treating bulimia comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 8.
30. A method of treating obesity and obesity-related disorders comprising the step of

administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1 in combination with one or more hypoglycemic agents.

31. The method of claim 30, wherein said hypoglycemic agent is selected from the group consisting of insulin, biguanidines, sulfonylureas, non-sulfonylurea secretagogues, insulin secretagogues, insulin sensitizers, α -glycosidase inhibitors, PPAR agonists, hepatic glucose output lowering compounds, and β_3 -adrenoreceptor agonists.
32. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 8 in combination with one or more hypoglycemic agents.
33. The method of claim 32, wherein said hypoglycemic agent is selected from the group consisting of insulin, biguanidines, sulfonylureas, non-sulfonylurea secretagogues, insulin secretagogues, insulin sensitizers, α -glycosidase inhibitors, PPAR agonists, hepatic glucose output lowering compounds, and β_3 -adrenoreceptor agonists.
34. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1 in combination with one or more agents that modulate digestion and/or metabolism.
35. The method of claim 34, wherein said agents that modulate digestion and/or metabolism include agents that modulate thermogenesis, lipolysis, gut motility, fat absorption, and satiety.
36. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 8 in combination with one or more agents that modulate digestion and/or metabolism.
37. The method of claim 36, wherein said agents that modulate digestion and/or metabolism include agents that modulate thermogenesis, lipolysis, gut motility, fat absorption, and satiety.
38. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof a therapeutically effective amount of a compound of claim 1 in combination with one or more agents selected from the group consisting of HMG CoA reductase inhibitor, bile acid binding agent, fibric acid derivative,

and agent that regulates hypertension.

39. A method of treating obesity and obesity-related disorders comprising the step of administering to a patient in need thereof therapeutically effective amount of a compound of claim 8 in combination with one or more agents selected from the group consisting of HMG CoA reductase inhibitor, bile acid binding agent, fibric acid derivative, and agent that regulates hypertension.
40. Compounds according to claims 1 or 8 for the treatment and/or prophylaxis of obesity and obesity-related disorders.
41. Medicaments containing at least one or more compounds according to claims 1 or 8 in combination with at least one pharmaceutically acceptable, pharmaceutically safe carrier or excipient.
42. Use of compounds according to claims 1 or 8 for manufacturing a medicament for the treatment and/or prophylaxis of obesity and obesity-related disorders.
43. Medicaments according to claim 41 for the treatment and/or prophylaxis of obesity and obesity-related disorders.

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